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=> d l4 1-61 ibib abs hitstr

L4   ANSWER 1 OF 61  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:586215  CAPLUS
TITLE:                    Pharmaceutical compositions based on anticholinergics
                          and additional active ingredients
INVENTOR(S):              Pairet, Michel; Pieper, Michael P.; Meade, Christopher
                          John Montague; Reichl, Richard; Schmelzer, Christel;
                          Jung, Birgit
PATENT ASSIGNEE(S):       Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SOURCE:                   U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S.
                          Ser. No. 824,391.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   14
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005148562	A1	20050707	US 2004-6940	20041208
DE 10062712	A1	20020620	DE 2000-10062712	20001215
DE 10063957	A1	20020627	DE 2000-10063957	20001220
DE 10110772	A1	20020912	DE 2001-10110772	20010307
DE 10111058	A1	20020912	DE 2001-10111058	20010308
DE 10113366	A1	20020926	DE 2001-10113366	20010320
DE 10138272	A1	20030227	DE 2001-10138272	20010810
US 2002151541	A1	20021017	US 2001-7182	20011019
US 2002183292	A1	20021205	US 2001-86145	20011019
US 2002137764	A1	20020926	US 2001-40196	20011025
US 2002122773	A1	20020905	US 2001-27662	20011220
DE 10206505	A1	20030828	DE 2002-10206505	20020216
US 2002169181	A1	20021114	US 2002-92116	20020306
US 6620438	B2	20030916		
US 2002193393	A1	20021219	US 2002-93240	20020307
US 2002183347	A1	20021205	US 2002-100659	20020318
US 6608054	B2	20030819		

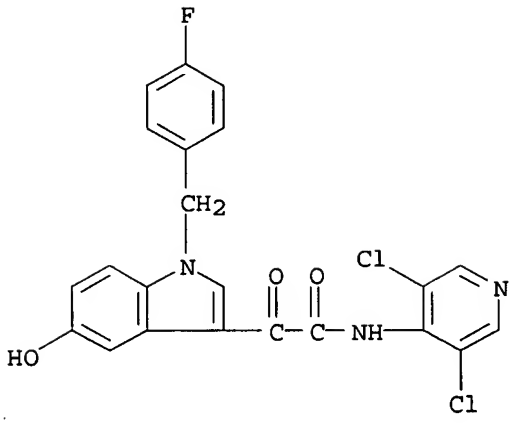
US 2003158196	A1	20030821	US 2003-360064		20030207
US 2003181478	A1	20030925	US 2003-395777		20030324
US 6890517	B2	20050510			
US 2003203925	A1	20031030	US 2003-413065		20030414
US 2003212075	A1	20031113	US 2003-419358		20030421
US 6696042	B2	20040224			
US 2004024007	A1	20040205	US 2003-613783		20030703
US 2004151770	A1	20040805	US 2004-763894		20040123
US 2004161386	A1	20040819	US 2004-775901		20040210
US 2004176338	A1	20040909	US 2004-776757		20040211
US 2004192675	A1	20040930	US 2004-824391		20040414
US 2005147564	A1	20050707	US 2005-68134		20050228
PRIORITY APPLN. INFO.:			DE 2000-10054042	A	20001031
			US 2000-253613P	P	20001128
			DE 2000-10062712	A	20001215
			DE 2000-10063957	A	20001220
			US 2000-257220P	P	20001221
			US 2000-257221P	P	20001221
			DE 2001-10110772	A	20010307
			DE 2001-10111058	A	20010308
			DE 2001-10113366	A	20010320
			US 2001-281653P	P	20010405
			US 2001-281857P	P	20010405
			US 2001-281874P	P	20010405
			DE 2001-10138272	A	20010810
			US 2001-314599P	P	20010824
			US 2001-7182	B1	20011019
			US 2001-86145	B1	20011019
			US 2001-27662	B1	20011220
			DE 2002-10206505	A	20020216
			US 2002-92116	A1	20020306
			US 2002-93240	B1	20020307
			US 2002-100659	A1	20020318
			US 2002-369213P	P	20020401
			US 2003-360064	A2	20030207
			US 2003-413065	B2	20030414
			US 2003-419358	A1	20030421
			US 2003-613783	A2	20030703
			US 2004-763894	A2	20040123
			US 2004-775901	A2	20040210
			US 2004-776757	A2	20040211
			US 2004-824391	A2	20040414
			US 2001-40196	B1	20011025
			US 2003-395777	A1	20030324

AB A pharmaceutical composition comprising an anticholinergic and at least one addnl. active ingredient selected from among corticosteroids, dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin antagonists, antihistamines, and EGFR-kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Among a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-[4-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide. Inhalable powders include a formulation containing tiotropium bromide, budesonide, and lactose.

IT **257892-33-4**, AWd-12-281
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. based on anticholinergics and addnl. active ingredients)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:409543 CAPLUS
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

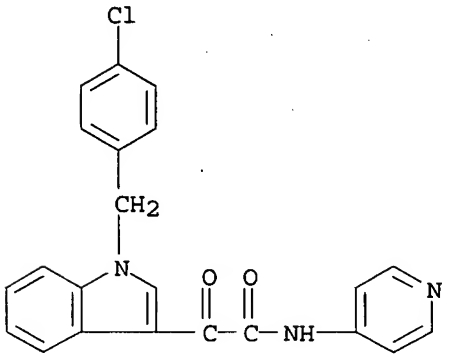
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148535	A1	20050707	US 2004-975974	20041028
PRIORITY APPLN. INFO.:			US 2003-516192P	P 20031030

AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their

effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

IT **204205-90-3**, D 24851
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:409357 CAPLUS
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119217	A1	20050602	US 2004-975790	20041028
PRIORITY APPLN. INFO.:			US 2003-516263P	P 20031030

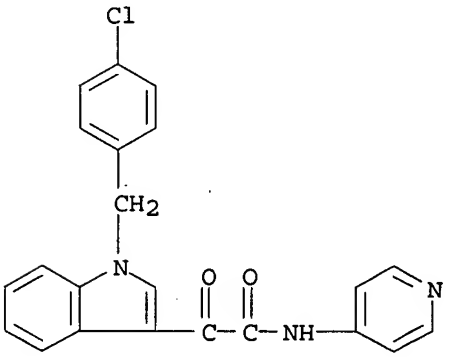
AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1

or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

IT **204205-90-3**, D 24851
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with chemotherapeutic agent)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:395031 CAPLUS

DOCUMENT NUMBER: 142:423824

TITLE: Improved combination bacteriolytic therapy for the treatment of tumors using spores of anaerobic bacteria and microtubule agents

INVENTOR(S): Dang, Long; Bettegowda, Chetan; Kinzler, Kenneth W.; Vogelstein, Bert

PATENT ASSIGNEE(S): The John Hopkins University, USA

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

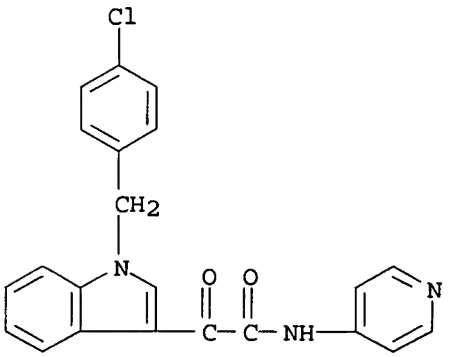
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005039492	A2	20050506	WO 2004-US34625	20041021

WO 2005039492 C2 20050602
WO 2005039492 A3 20050630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-512923P P 20031022

AB Current approaches for treating cancer are limited, in part, by the inability of drugs to affect the poorly vascularized regions of tumors. We have found that spores of anaerobic bacteria in combination with agents which interact with microtubules can cause the destruction of both the vascular and avascular compartments of tumors. Two classes of microtubule inhibitors were found to exert markedly different effects. Some agents that inhibited microtubule synthesis, such as vinorelbine, caused rapid, massive hemorrhagic necrosis when used in combination with spores. In contrast, agents that stabilized microtubules, such as the taxane docetaxel, resulted in slow tumor regressions that killed most neoplastic cells. Remaining cells in the poorly perfused regions of tumors could be eradicated by sponzlated bacteria. Mechanistic studies showed that the microtubule destabilizers, but not the microtubule stabilizers, radically reduced blood flow to tumors, thereby enlarging the hypoxic niche in which spores could germinate. A single i.v. injection of spores plus selected microtubule-interacting agents was able to cause regressions of several tumors in the absence of excessive toxicity.

IT **204205-90-3**, D-24851
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination bacteriolytic therapy for the treatment of tumors using spores of anaerobic bacteria and microtubule agents)

RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:324038 CAPLUS
DOCUMENT NUMBER: 142:397825
TITLE: Biocompatible, biostable coating of medical surfaces composed of polysulfone and hydrophilic polymers
INVENTOR(S): Horres, Roland; Hoffmann, Michael; Faust, Volker;

Hoffmann, Erika; Di Biase, Donato
PATENT ASSIGNEE(S): Hemoteq G.m.b.H., Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005032611	A2	20050414	WO 2004-DE2184	20040929
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004020856	A1	20050414	DE 2004-102004020856	20040428
US 2005129731	A1	20050616	US 2004-979977	20041103

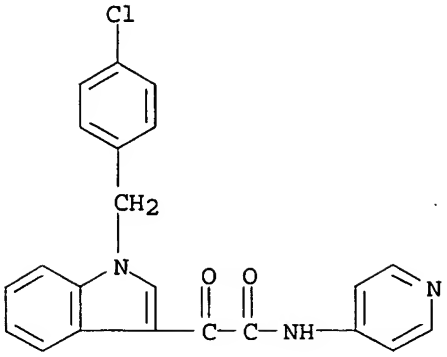
PRIORITY APPLN. INFO.:
DE 2003-10345132 A 20030929
US 2003-516295P P 20031103
DE 2004-102004020856A 20040428
US 2004-571582P P 20040517

AB The invention relates to medical products comprising at least one biocompatible biostable polysulfone coating. Said polysulfone coating makes it possible, via the admixt. of an adequate quantity of at least one hydrophilic polymer, to control the elution kinetics of the at least one antiproliferative, anti-inflammatory, antiphlogistic, and/or antithrombogenic agent that is introduced and/or applied while allowing different agents or agent concns. to be spatially separated with the aid of the layer system of biostable polymers. Also disclosed are a method for producing said medical products and the use thereof particularly in the form of stents for preventing restenosis. Thus a 2 g base-coat solution for spray coating contained 17.6 mg polyethersulfone(Udel form Solvay) in chloroform. The 3 g chloroformic topcoat solution included 25.2 g polyethersulfone and 1,2 mg PVP.

IT **204205-90-3**, D-24851
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biocompatible, biostable coating of medical surfaces composed of polysulfone and hydrophilic polymers)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:283298 CAPLUS
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916

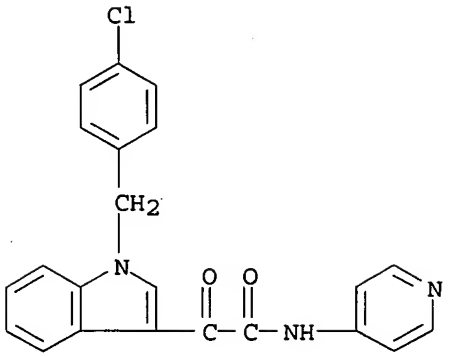
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT **204205-90-3**, D 24851
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorpromazine compound-antiproliferative drug antitumor combination)

RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)

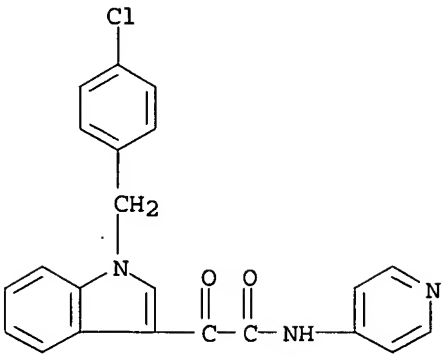


L4 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:243925 CAPLUS
DOCUMENT NUMBER: 142:423274
TITLE: Microtubule inhibitor D-24851 induces p53-independent apoptotic cell death in malignant glioma cells through Bcl-2 phosphorylation and Bax translocation
AUTHOR(S): Ito, Hideaki; Kanzawa, Takao; Kondo, Seiji; Kondo, Yasuko
CORPORATE SOURCE: Department of Neurosurgery, Anderson Cancer Center, The University of Texas M.D., Houston, TX, 77030, USA
SOURCE: International Journal of Oncology (2005), 26(3), 589-596
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB D-24851 is a recently developed microtubule inhibitor that induces G2/M cell-cycle arrest and has an antitumor effect in many cancer cell types. It is expected to be a promising chemotherapeutic agent against a broad range of tumors. However, the precise mechanisms underlying its antitumor effect remain to be determined Here, we investigated the in vitro effect of D-24851 on tumor growth and the apoptosis mechanism in human malignant glioma cells. Because both p53-dependent and -independent pathways of apoptosis have been reported, we used cell lines with wildtype p53 (U87-MG and D54) and cell lines with mutant p53 (U373-MG and T98G) and compared their responses to D-24851. D-24851 substantially inhibited the proliferation of the four glioma cell lines tested in a dose- and time-dependent manner. The inhibitory effect of D-24851 on tumor growth was associated with cell-cycle arrest in G2/M, subsequently inducing apoptosis. D-24851 treatment induced phosphorylated Bcl-2 and translocated Bax from the cytoplasm to the mitochondria, resulting in apoptotic cell death. These events took place regardless of the p53 status of tumor cells. Our results indicated that D-24851 effectively induces apoptosis through Bcl-2 phosphorylation and Bax translocation in human malignant glioma cells in a p53-independent manner. The results of this study make D-24851 even more promising as a therapeutic agent, especially because many malignant gliomas have a heterogeneous p53 status.

IT **204205-90-3**, D-24851
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D-24851 showed dose, time dependent inhibition of cell proliferation by Bcl-2 phosphorylation and Bax translocation, induced p53-independent apoptosis in U373-MG, U87-MG human malignant glioma cell line)

RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)

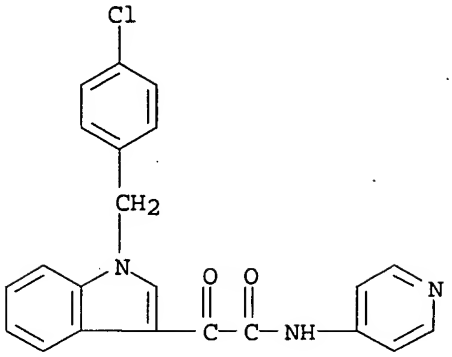


REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

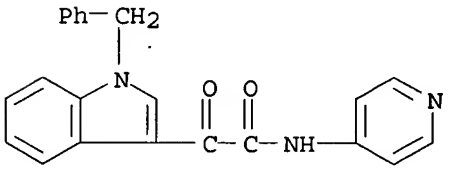
L4 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:144032 CAPLUS
DOCUMENT NUMBER: 142:388504
TITLE: Stable isotopically labeled internal standards in quantitative bioanalysis using liquid chromatography/mass spectrometry: necessity or not?
AUTHOR(S): Stokvis, Ellen; Rosing, Hilde; Beijnen, Jos H.
CORPORATE SOURCE: Department of Pharmacy & Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.
SOURCE: Rapid Communications in Mass Spectrometry (2005), 19(3), 401-407
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It appears to be a general belief that stable isotopically labeled (SIL) internal stds. yield better assay performance results for quant. bioanal. liquid chromatog./mass spectrometry (LC/MS) assays than does any other internal standard In this article we describe our experiences with structural analogs and SIL internal stds. and their merits and demerits. SIL internal stds. are the first choice, but deuterium-labeled compds. may demonstrate unexpected behavior, such as different retention times or recoveries, than the analyte. In addition, a SIL internal standard with identical chemical properties as the analyte may cover up assay problems with stability, recovery, and ion suppression. Since SIL internal stds. are not always available or are very expensive, structural analogs can be used, however, with consideration of several issues, which are usually displayed during method validation.

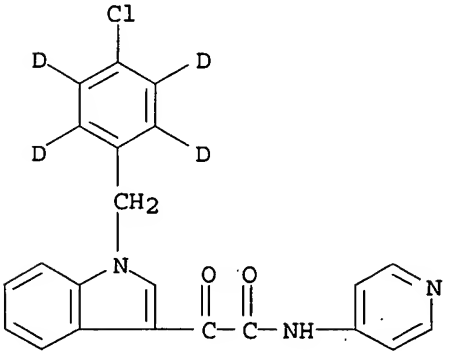
IT **204205-90-3**, D-24851
RL: ANT (Analyte); ANST (Analytical study)
(stable isotopically labeled internal stds. in quant. bioanal. using liquid chromatog./mass spectrometry)
RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



IT **204205-86-7 849674-89-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (stable isotopically labeled internal stds. in quant. bioanal. using liquid chromatog./mass spectrometry)
RN 204205-86-7 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-1-(phenylmethyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 849674-89-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl-2,3,5,6-d4)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136543 CAPLUS
DOCUMENT NUMBER: 142:246142
TITLE: Medicaments comprising PDE IV inhibitors and an anticholinergic agent for treating respiratory disorders
INVENTOR(S): Germeyer, Sabine; Meade, Christopher John Montague; Meissner, Helmut; Morschhaeuser, Gerd; Pairet, Michel;

Pestel, Sabine; Pieper, Michael P.; Pohl, Gerald; Reichl, Richard; Speck, Georg
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013967	A1	20050217	WO 2004-EP8003	20040723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005043343	A1	20050224	US 2004-891562	20040715

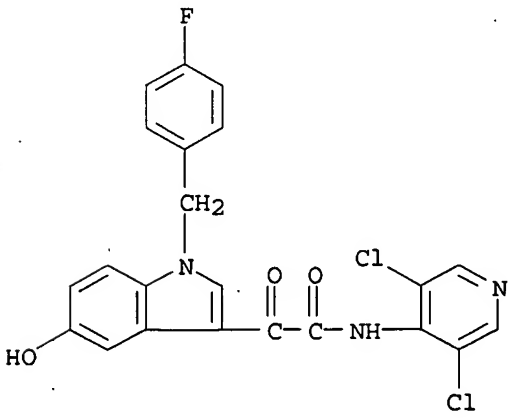
PRIORITY APPLN. INFO.: EP 2003-17039 A 20030728
US 2003-508119P P 20031002
OTHER SOURCE(S): MARPAT 142:246142

AB The present invention relates to pharmaceutical compns. based on PDE IV inhibitors and salts of a novel anticholinergic, processes for preparing them and their use in the treatment of respiratory complaints. For example, scopine 9-methylfluorene-9-carboxylate methobromide was prepared and formulated into inhalable powder containing the drug 80 μg, AWD-12-281 200 μg, and lactose 12220 μg per capsule.

IT **257892-33-4**, AWD 12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GW-842470; inhalable compns. comprising anticholinergic agent and PDE IV inhibitors for treating respiratory disorders)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

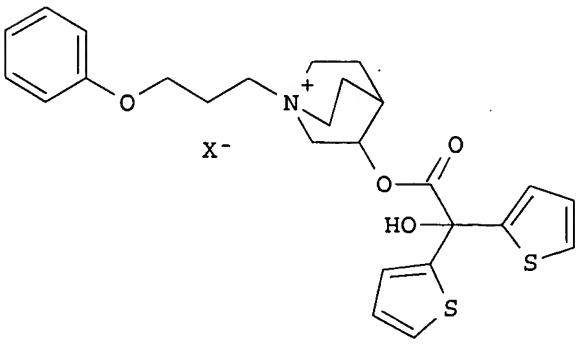
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:99152 CAPLUS
DOCUMENT NUMBER: 142:204737
TITLE: Medicaments for inhalation comprising an anticholinergic and a PDE IV inhibitor
INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michel; Pieper, Michael P.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026886	A1	20050203	US 2004-891551	20040715
WO 2005013993	A1	20050217	WO 2004-EP8024	20040717

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-17164 A 20030729
US 2003-508125P P 20031002
OTHER SOURCE(S): MARPAT 142:204737
GI



I

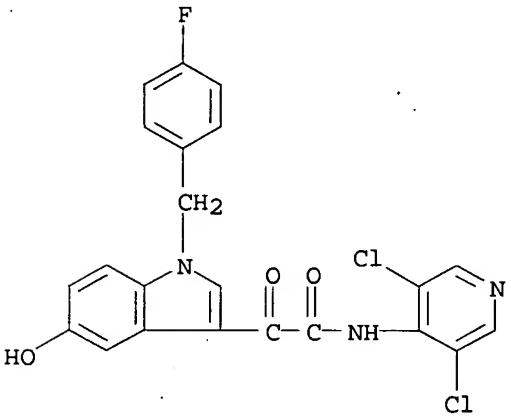
AB A pharmaceutical composition comprises: (a) a compound of formula I wherein X- is an anion with a single neg. charge; and (b) a PDE IV inhibitor, or an enantiomer, mixture of enantiomers, racemate, solvate, or hydrate thereof. A processes for preparing them, and their use in the treatment of respiratory complaints is also disclosed. A suspension aerosol contained I bromide 0.050, AWD-12-281 0.060, soya lecithin 0.2 and TG 134a:TG 227 (2:3) q.s.

100%.

IT **257892-33-4**, AWD-12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments for inhalation comprising anticholinergic and PDE IV inhibitor)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



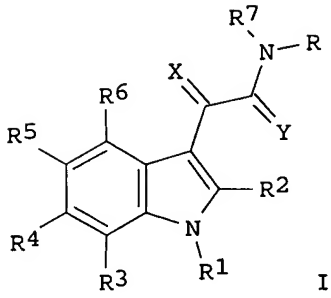
L4 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1080885 CAPLUS
DOCUMENT NUMBER: 142:56172
TITLE: Preparation of 1-(4-chlorobenzyl)indoles as tubulin polymerization inhibitors with apoptosis inducing activity
INVENTOR(S): Gerlach, Matthias; Schuster, Tilmann; Emig, Peter; Schmidt, Peter; Bassner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108702	A1	20041216	WO 2004-EP5593	20040525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1484329	A1	20041208	EP 2003-12868	20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

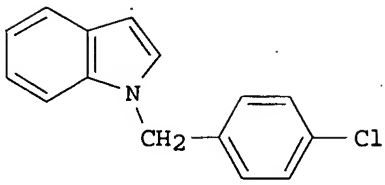
PRIORITY APPLN. INFO.: US 2003-476277P P 20030605

EP 2003-12868 A 20030606
EP 2004-11598 A 20040515

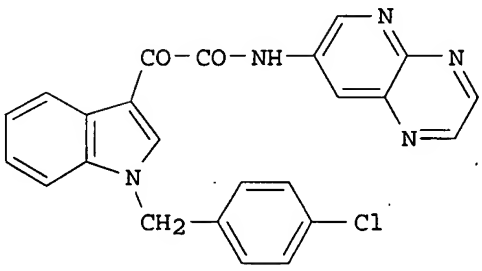
GI



I



II



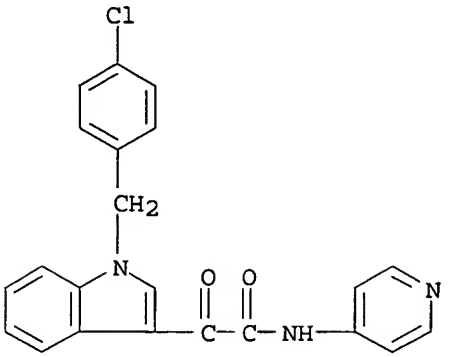
III

AB Title comounds I [R = (un)substituted heterocycle containing N, O, S heteroatoms; R1 = (un)substituted alkyl-aryl; R2 = H, (un)substituted alkyl; R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, etc.; R7 = alkylcarbonyl, alkoxycarbonyl; X, Y = S, O] and their pharmaceutically acceptable salts were prepared For example, oxalyl chloride acylation of chlorobenzylindole II, i.e., prepared from indole and 4-chlorobenzyl chloride, followed by pyrido[2,3-b]pyrazin-7-amine amidation afforded claimed chlorobenzylindole III in 68% yield. In human tubulin polymerization inhibition assays, 4-examples of compds. I exhibited EC50 values ranging from 0.71-1.26 μg/mL, i.e., the EC50 value of chlorobenzylindole III was 0.71 μg/mL. Compds. I are claimed to be useful as antitumor agents.

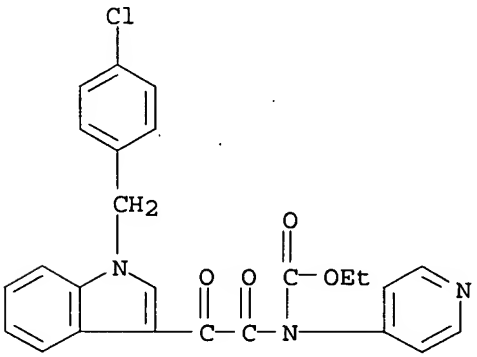
IT **204205-90-3P**, 2-[1-(4-Chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-ylacetamide **808580-26-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of chlorobenzylindoles as tubulin polymerization inhibitors with
apoptosis inducing activity)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 808580-26-9 CAPLUS
CN Carbamic acid, [[1-[(4-chlorophenyl)methyl]-1H-indol-3-yl]oxoacetyl]-4-pyridinyl-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1036929 CAPLUS
DOCUMENT NUMBER: 142:16825
TITLE: Composition comprising a PDE4 inhibitor and a PDE5 inhibitor
INVENTOR(S): Dunkern, Thorsten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein Ardeschir
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

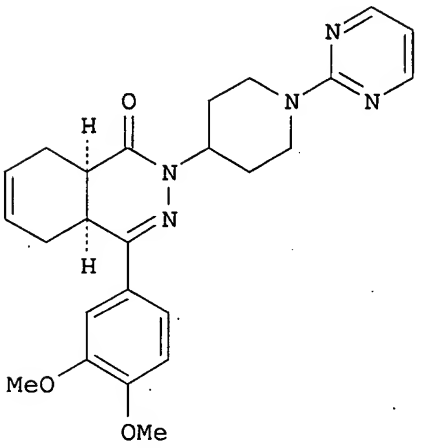
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103407	A2	20041202	WO 2004-EP50869	20040519
WO 2004103407	A3	20050217		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-11609 A 20030522

GI



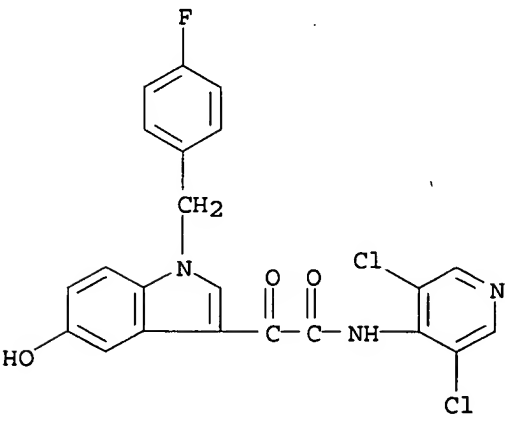
I

AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is I.

IT **257892-33-4**, AWD-12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and a PDE5 inhibitor)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:996001 CAPLUS
DOCUMENT NUMBER: 141:406065
TITLE: Composition comprising a PDE-4 inhibitor and a TNF-alpha antagonist
INVENTOR(S): Barsig, Johannes; Weimar, Christian
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098633	A1	20041118	WO 2004-EP50748	20040510

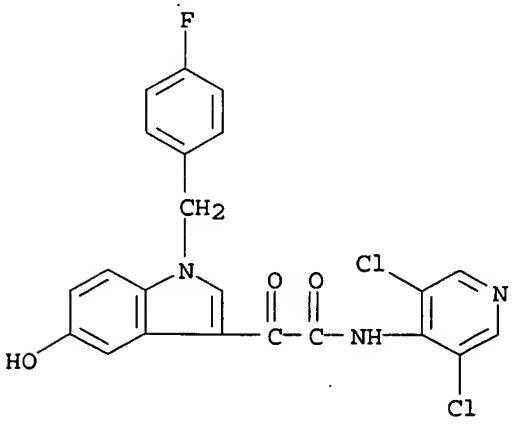
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10581 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and a TNFα antagonist selected from the group consisting of etanercept, onercept and pegsunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNFα) activity is detrimental.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic activity of phosphodiesterase 4 inhibitors and TNFα antagonists)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995979 CAPLUS
DOCUMENT NUMBER: 141:406064
TITLE: Composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098606	A1	20041118	WO 2004-EP50749	20040510

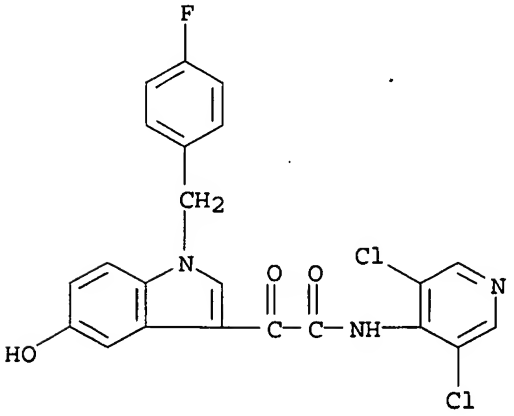
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10596 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and shuIL-1R II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental. .

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995978 CAPLUS
DOCUMENT NUMBER: 141:406063
TITLE: Pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098605	A1	20041118	WO 2004-EP50747	20040510

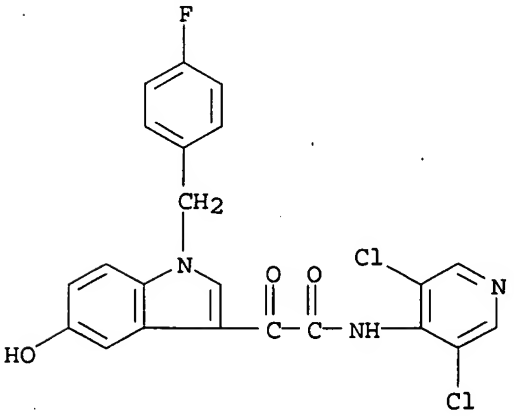
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10631 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:927194 CAPLUS
DOCUMENT NUMBER: 141:395426
TITLE: Preparation of N-oxopyridinyl hydroxyindolylglyoxylamides as phosphodiesterase IV inhibitors.
INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Steinike, Karin; Egerland, Ute; Rundfeldt, Chris; Pfeifer, Thomas
PATENT ASSIGNEE(S): Elbion A.-G., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094406	A1	20041104	WO 2004-EP4340	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10318609	A1	20041111	DE 2003-10318609	20030424
US 2004266760	A1	20041230	US 2004-824342	20040414
PRIORITY APPLN. INFO.:			DE 2003-10318609 A	20030424
OTHER SOURCE(S):	MARPAT 141:395426			

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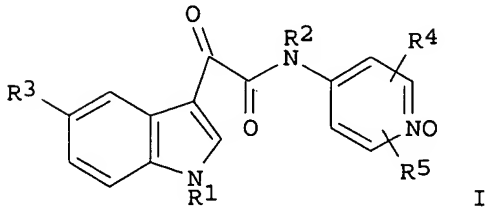
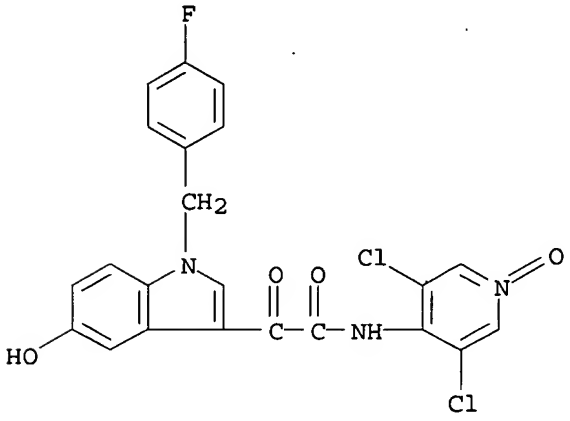


I

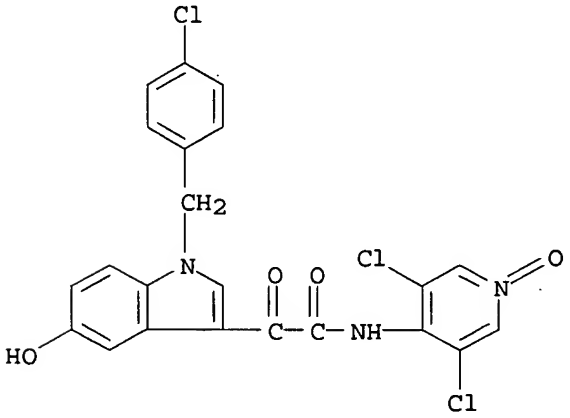
AB Title compds. [I; R1 = (substituted) alkyl, alkenyl; R2 = H, alkyl; R3 = OH; R4, R5 = H, alkyl, OH, SH, NH2, NO2, cyano, SO3H, CO2H, alkoxycarbonyl, halo, alkoxy, alkylthio, (substituted) Ph, pyridyl, etc.], were prepared Thus, N-(3,5-dichloropyridin-4-yl) [5-benzyloxy-1-(4-fluorobenzyl)indol-3-yl]glyoxylamide in CH2Cl2 was treated dropwise with m-chloroperbenzoic acid in HOAc followed by stirring for 7 days to give 16.1% pyridine N-oxide derivative, which was refluxed with BBr3 in CH2Cl2 to give 72.8% N-(3,5-dichloro-1-oxopyridin-4-yl) [1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]glyoxylamide. I inhibited phosphodiesterase 4 with IC50's in the range of 10-5 M to 10-10 M.

IT **786688-50-4P 786688-51-5P 786688-52-6P**
786688-53-7P 786688-54-8P 786688-55-9P
786688-56-0P 786688-57-1P 786688-58-2P
786688-59-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of oxopyridinyl hydroxyindolylglyoxylamides as
phosphodiesterase IV inhibitors)

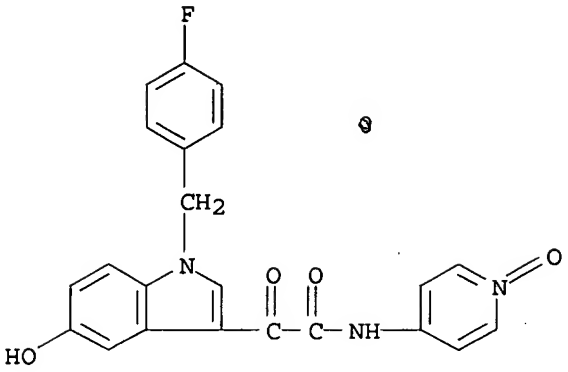
RN 786688-50-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



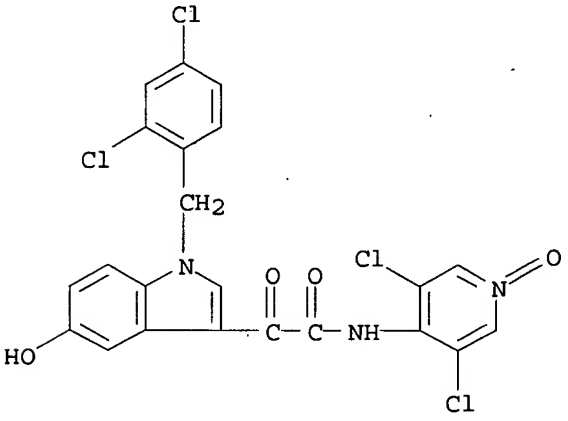
RN 786688-51-5 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-N-(3,5-dichloro-1-oxido-4-pyridinyl)-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



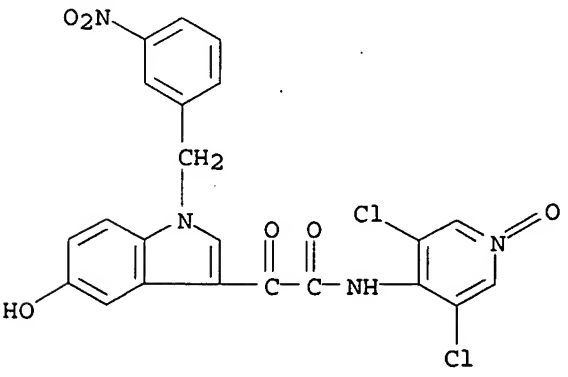
RN 786688-52-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-hydroxy-N-(1-oxido-4-pyridinyl)-α-oxo- (9CI) (CA INDEX NAME)



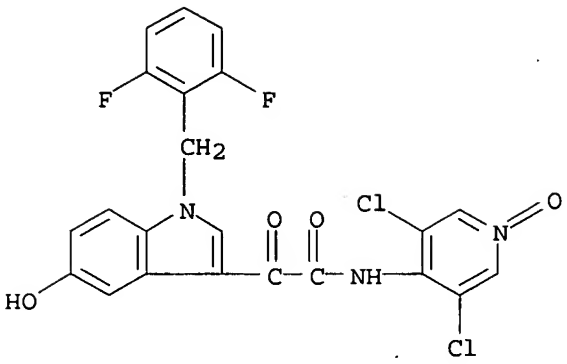
RN 786688-53-7 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(2,4-dichlorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



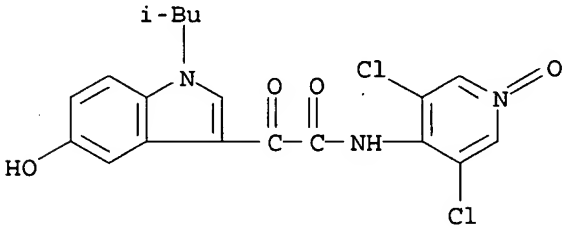
RN 786688-54-8 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-5-hydroxy-1-[(3-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



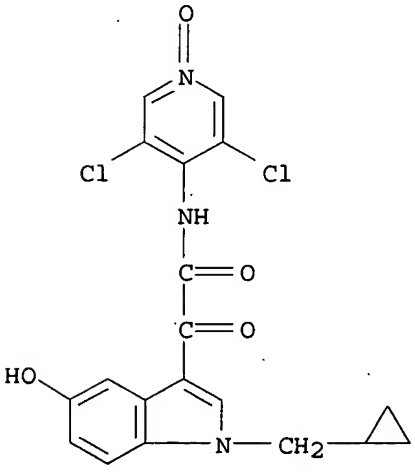
RN 786688-55-9 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



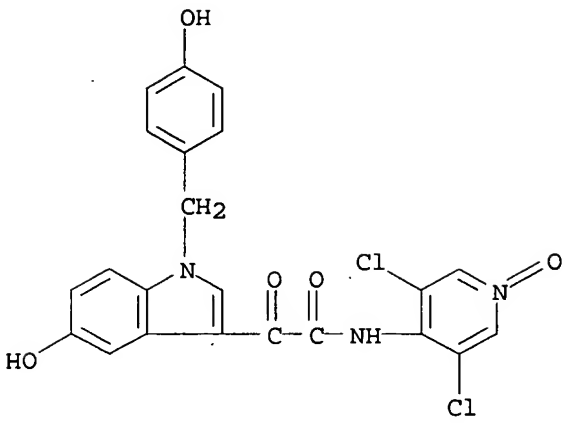
RN 786688-56-0 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-5-hydroxy-1-(2-methylpropyl)-α-oxo- (9CI) (CA INDEX NAME)



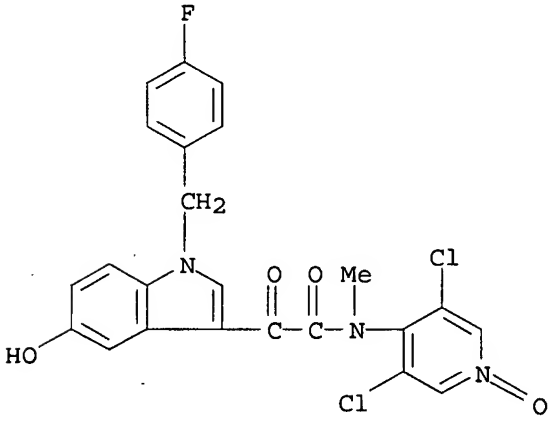
RN 786688-57-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-(cyclopropylmethyl)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



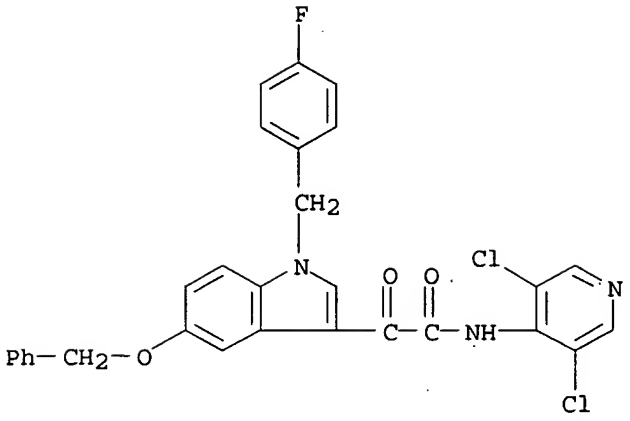
RN 786688-58-2 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-5-hydroxy-1-[(4-hydroxyphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



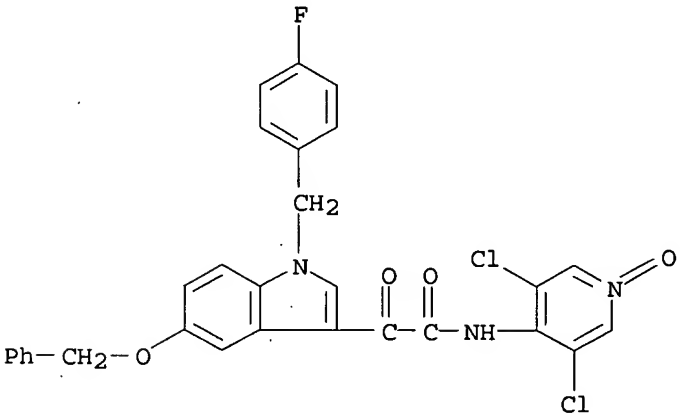
RN 786688-59-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-N-methyl-α-oxo- (9CI) (CA INDEX NAME)



IT **656237-85-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxopyridinyl hydroxyindolylglyoxylamides as phosphodiesterase IV inhibitors)
RN 656237-85-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



IT **786688-60-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of oxopyridinyl hydroxyindolylglyoxylamides as phosphodiesterase IV inhibitors)
RN 786688-60-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:927193 CAPLUS
DOCUMENT NUMBER: 141:395425
TITLE: Preparation of hydroxyindolylglyoxylic acid oxopyridinylamides as phosphodiesterase IV inhibitors.
INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Steinike, Karin; Egerland, Ute; Rundfeldt, Chris
PATENT ASSIGNEE(S): Elbion A.-G., Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094405	A1	20041104	WO 2004-EP4338	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10318611	A1	20041111	DE 2003-10318611	20030424
US 2004242643	A1	20041202	US 2004-825862	20040416
PRIORITY APPLN. INFO.:			DE 2003-10318611 A	20030424
OTHER SOURCE(S):	MARPAT 141:395425			

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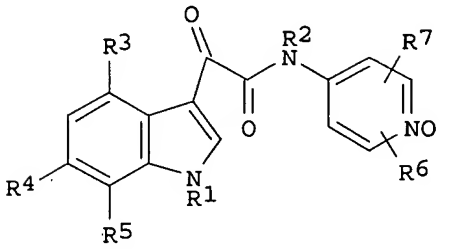


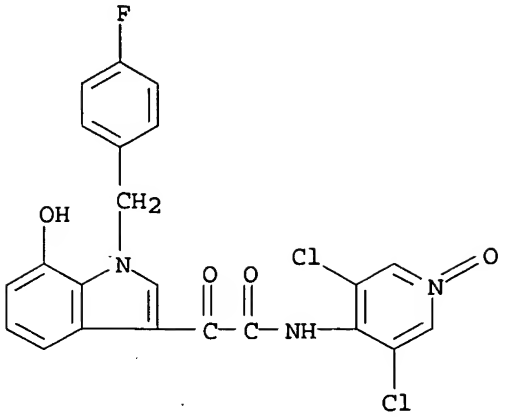
I

AB Title compds. [I; R1 = (substituted) alkyl, alkenyl; R2 = H, alkyl; R3-R5 = H, OH; ≥1 or R3-R5 = OH; R6, R7 = H, alkyl, OH, SH, NH2, NO2, cyano, SO3H, CO2H, alkylcarbonyloxy, halo, alkylthio, (substituted) Ph, pyridyl, etc.], were prepared Thus, N-(3,5-dichloropyridin-4-yl) [7-benzyloxy-1-(4-fluorobenzyl)indol-3-yl]glyoxylic acid amide was stirred 7 days with m-chloroperbenzoic acid in HOAc to give 16.9% pyridine N-oxide derivative, which was refluxed with BBr3 in CH2Cl2 to give 66.2% N-(3,5-dichloro-1-oxopyridin-4-yl) [1-(4-fluorobenzyl)-7-hydroxyindol-3-yl]glyoxylic acid amide. I inhibited phosphodiesterase 4 with IC50's in the range of 10-10 M to 10-5 M.

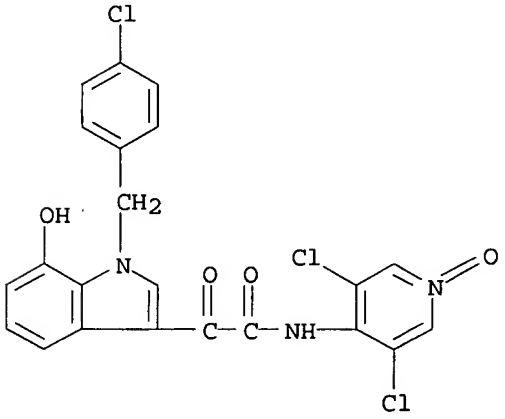
IT **785787-52-2P 785787-53-3P 785787-54-4P**
785787-55-5P 785787-56-6P 785787-57-7P
785787-58-8P 785787-59-9P 785787-60-2P
785787-61-3P 785787-62-4P 785787-63-5P
785787-64-6P 785787-65-7P 785787-66-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of hydroxyindolylglyoxylic acid oxopyridinylamides as phosphodiesterase IV inhibitors)

RN 785787-52-2 CAPLUS

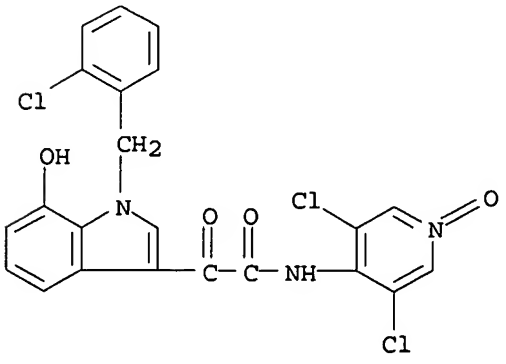
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 785787-53-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

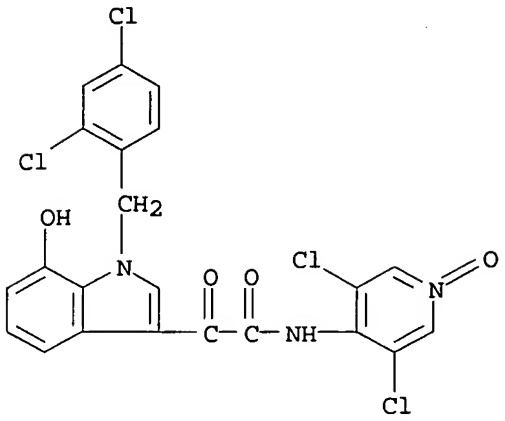


RN 785787-54-4 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chlorophenyl)methyl]-N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

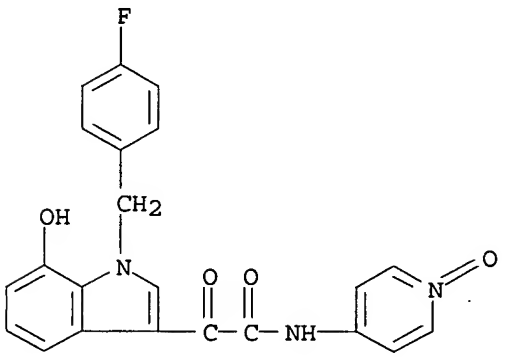


RN 785787-55-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(2,4-

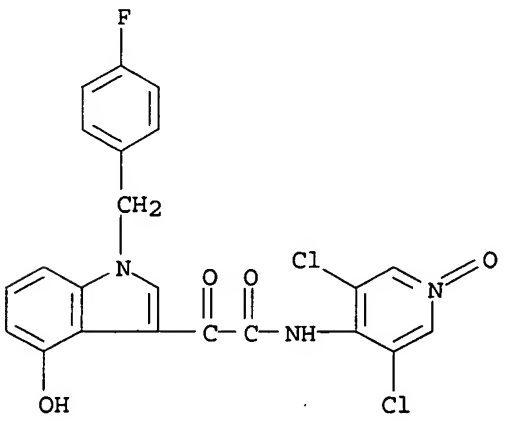
dichlorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 785787-56-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-7-hydroxy-N-(1-oxido-4-pyridinyl)-α-oxo- (9CI) (CA INDEX NAME)

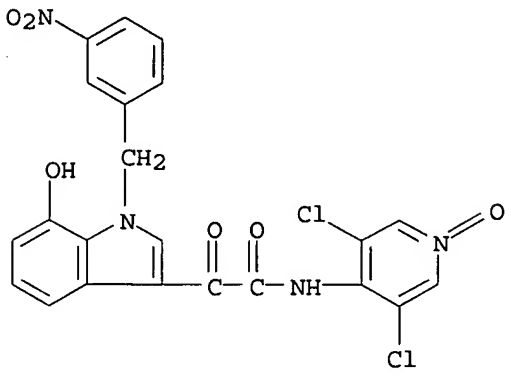


RN 785787-57-7 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-4-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

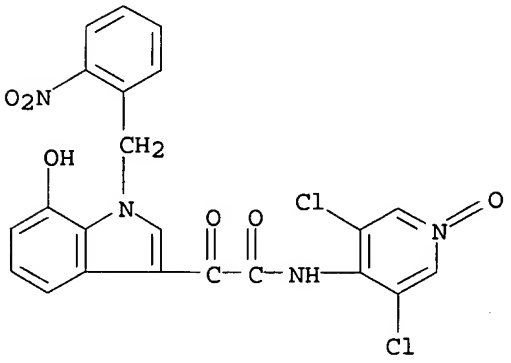


RN 785787-58-8 CAPLUS

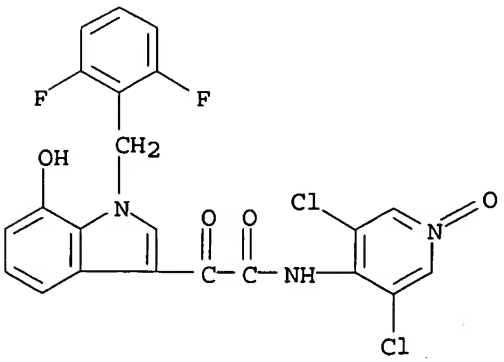
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-1-[(3-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



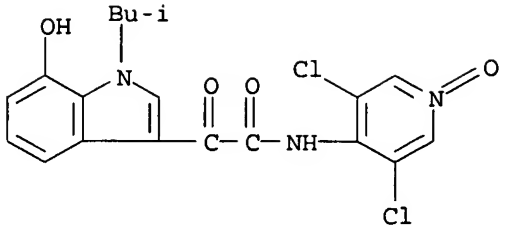
RN 785787-59-9 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-1-[(2-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



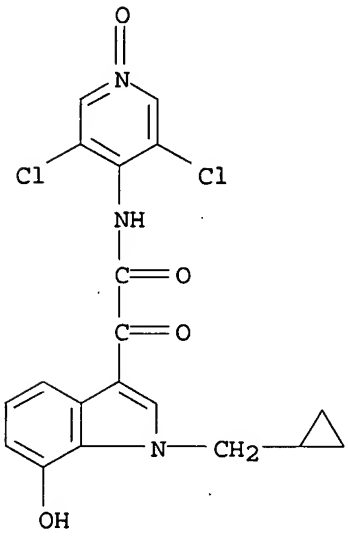
RN 785787-60-2 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



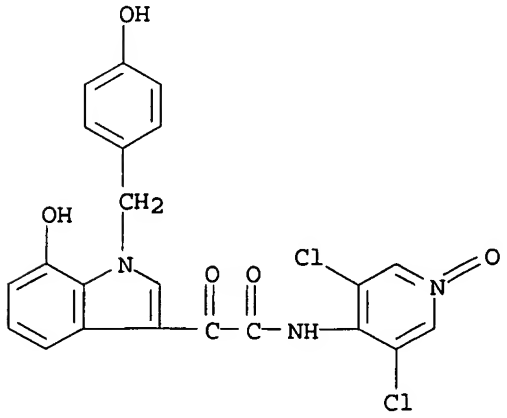
RN 785787-61-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-1-(2-methylpropyl)-α-oxo- (9CI) (CA INDEX NAME)



RN 785787-62-4 CAPLUS
CN 1H-Indole-3-acetamide, 1-(cyclopropylmethyl)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

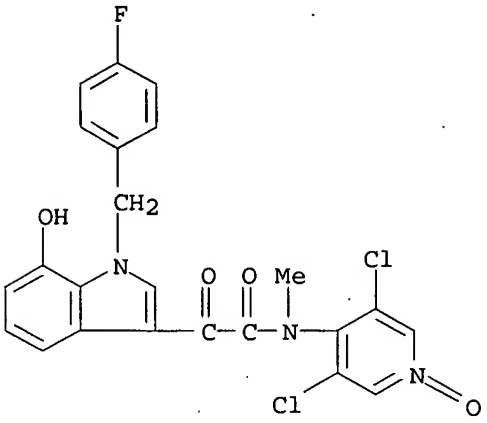


RN 785787-63-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-7-hydroxy-1-[(4-hydroxyphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)

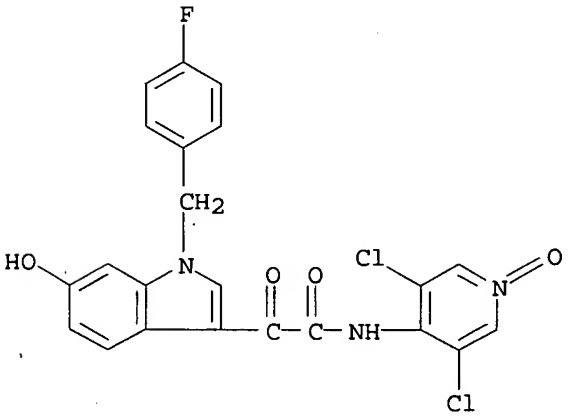


RN 785787-64-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-

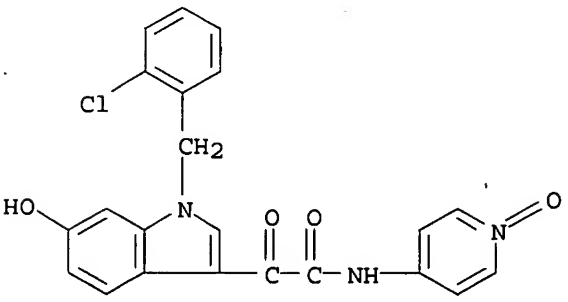
fluorophenyl)methyl]-7-hydroxy-N-methyl-α-oxo- (9CI) (CA INDEX NAME)



RN 785787-65-7 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-6-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 785787-66-8 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chlorophenyl)methyl]-6-hydroxy-N-(1-oxido-4-pyridinyl)-α-oxo- (9CI) (CA INDEX NAME)

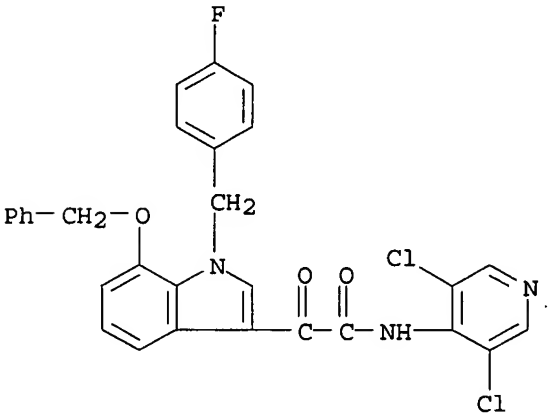


IT **785787-68-0**
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of hydroxyindolylglyoxylic acid oxopyridinylamides as phosphodiesterase IV inhibitors)

RN 785787-68-0 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)



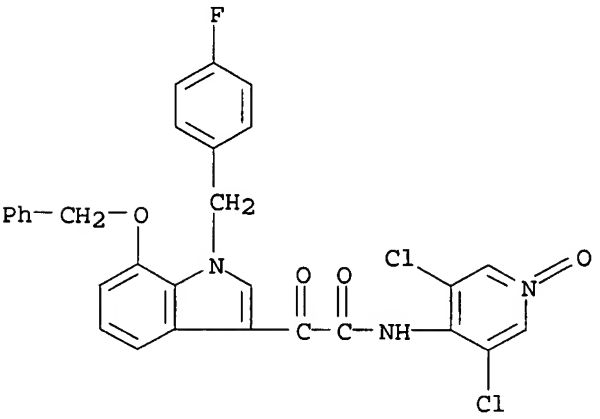
IT **785787-67-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxyindolylglyoxylic acid oxopyridinylamides as phosphodiesterase IV inhibitors)

RN 785787-67-9 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:610086 CAPLUS

DOCUMENT NUMBER: 141:134069

TITLE: PDE4 inhibitors for the treatment of neoplasms of lymphoid cells

INVENTOR(S): Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker; Sanders, Karl; Garattini, Enrico; Braunger, Juergen; Schudt, Christian

PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062671	A2	20040729	WO 2004-EP196	20040114
WO 2004062671	A3	20050127		

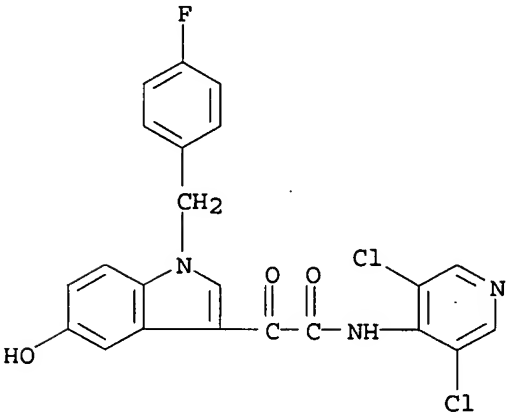
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRIORITY APPLN. INFO.: EP 2003-787 A 20030114
OTHER SOURCE(S): MARPAT 141:134069

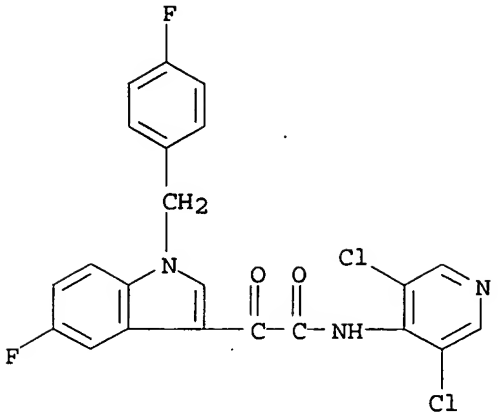
AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concns. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the treatment of neoplasms of lymphoid cells.

IT **257892-33-4**, AWD-12-281 **444659-44-3**, AWD-12-343
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



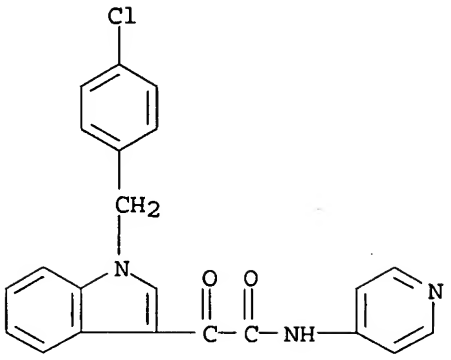
RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:565834 CAPLUS
DOCUMENT NUMBER: 141:98938
TITLE: Quantitative analysis of D-24851, a novel anticancer agent, in human plasma and urine by liquid chromatography coupled with tandem mass spectrometry
AUTHOR(S): Stokvis, Ellen; Nan-Offeringa, Lianda G. A. H.; Ouwehand, Mariet; Tibben, Matthijs M.; Rosing, Hilde; Schnaars, Yvonne; Grigat, Martina; Romeis, Peter; Schellens, Jan H. M.; Beijnen, Jos H.
CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.
SOURCE: Rapid Communications in Mass Spectrometry (2004), 18(13), 1465-1471
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of a liquid chromatog./tandem mass spectrometric assay for the quant. anal. of the novel tubulin inhibitor D-24851 in human plasma and urine is described. D-24851 and the deuterated internal standard were extracted from 250 μL of plasma or urine using hexane/ether (1:1, volume/volume). Subsequently, 10-μL aliquots of reconstituted exts. were injected onto an Inertsil ODS anal. column (50 + 2.0 mm internal diameter, 5 μm particle size). An eluent consisting of MeOH/5 mM ammonium acetate, 0.004% formic acid in H2O (80:20, volume/volume) was pumped at a flow rate of 0.2 mL/min. An API 365 triple quadrupole mass spectrometer was used in the multiple reaction monitoring mode for sensitive detection. For human plasma a dynamic range of 1-1000 ng/mL was validated, and for human urine a range of 0.25-50 ng/mL. Validation was performed according to the most recent FDA guidelines and all results were within requirements. The assay was successfully applied to support a phase I clin. trial with orally administered D-24851.

IT **204205-90-3**, D-24851
RL: ANT (Analyte); ANST (Analytical study)
(quant. anal. of D-24851, a novel anticancer agent, in human plasma and urine by liquid chromatog. coupled with tandem mass spectrometry)
RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:467725 CAPLUS
DOCUMENT NUMBER: 141:17651
TITLE: Phosphodiesterase IV and phosphodiesterase III/IV inhibitors for use in the treatment of cachexia
INVENTOR(S): Schmidt, Mathias
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047817	A1	20040610	WO 2003-EP13313	20031126

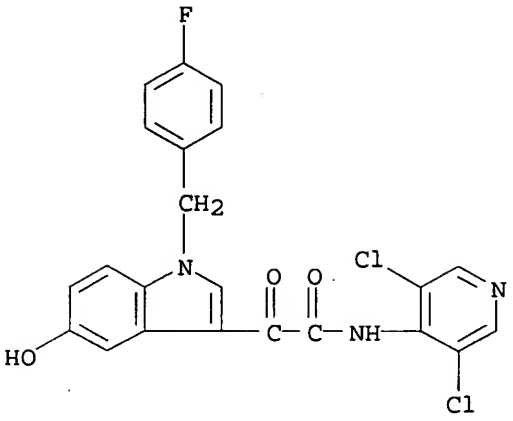
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, EG, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: EP 2002-26548 A 20021127

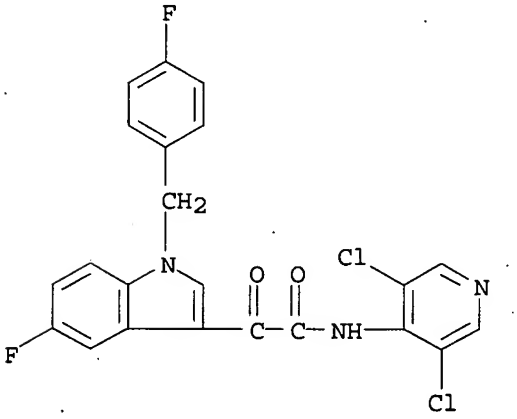
AB The invention discloses the use of a PDE IV or PDE III/IV inhibitor for the treatment of cachexia.

IT **257892-33-4 444659-44-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV and phosphodiesterase III/IV inhibitors for treatment of cachexia)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)

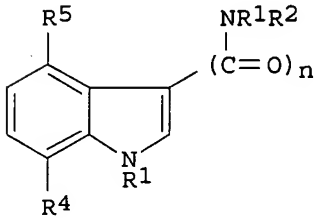


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:450478 CAPLUS
DOCUMENT NUMBER: 141:23423
TITLE: Preparation of 4- and/or 7-hydroxyindoles as phosphodiesterase 4 inhibitors
INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Egerland, Ute; Rundfeldt, Chris; Hartenhauer, Helge; Gasparic, Antje
PATENT ASSIGNEE(S): Elbion Ag, Germany
SOURCE: Ger. Offen., 17 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10253426	A1	20040603	DE 2002-10253426	20021115
US 2004147759	A1	20040729	US 2003-714568	20031113

WO 2004045607 A1 20040603 WO 2003-EP12742 20031114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: DE 2002-10253426 A 20021115
OTHER SOURCE(S): MARPAT 141:23423
GI



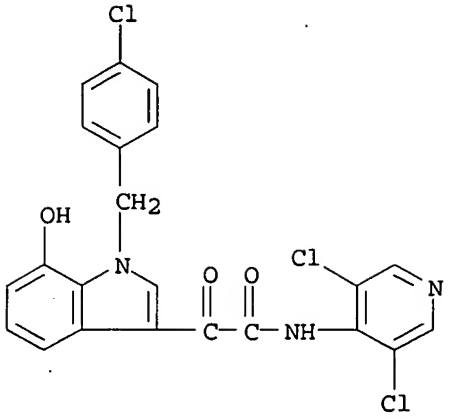
I

AB Title compds. [I; n = 1, 2; R1 = (substituted) (branched) alkyl, (substituted) (branched) unsatd. alkenyl; R2, R3 = H, (substituted) alkyl, pyridyl, etc.; R4, R5 = H, OH], were prepared Thus, a suspension of NaH in THF was dropwise treated with 4-amino-3,5-dichloropyridine in THF followed by stirring for 1 h at 20°. The reaction mixture was dropwise treated with 7-benzyloxy-1-(4-chlorobenzyl)-indol-3-ylglyoxyloyl chloride (preparation given) at 0° followed by reflux for 4 h to give 47.5% N-(3,5-dichloropyridin-4-yl)-[1-(4-chlorobenzyl)-7-hydroxyindol-3-yl]glyoxylamide. The latter inhibited phosphodiesterase 4 (PDE 4) with IC50 = 0.002 μmol/L.

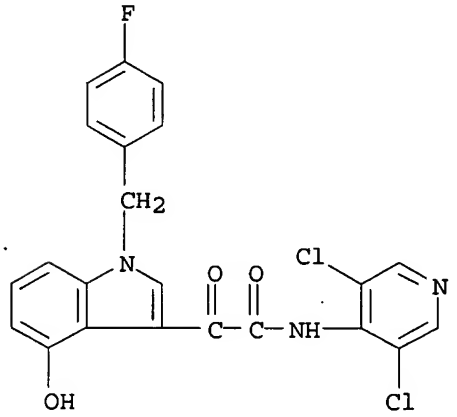
IT **697747-46-9P 697747-50-5P 697747-51-6P**
697747-52-7P 697747-53-8P 697747-54-9P
697747-55-0P 697747-56-1P 697747-57-2P
697747-58-3P 697747-59-4P 697747-60-7P
697747-61-8P 697747-62-9P 697747-65-2P
697747-66-3P 697747-68-5P 697747-69-6P
697747-70-9P 697747-71-0P 697747-72-1P
697747-73-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxyindoles as phosphodiesterase 4 inhibitors)

RN 697747-46-9 CAPLUS

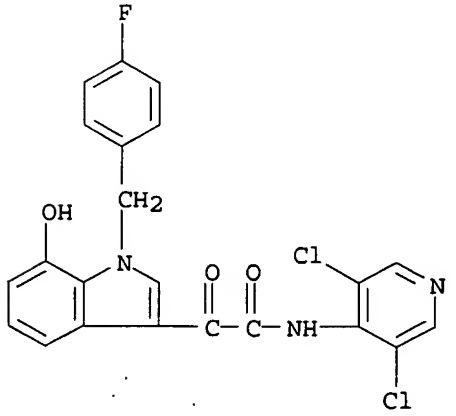
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



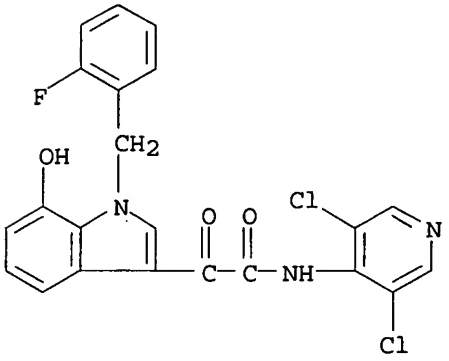
RN 697747-50-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-4-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



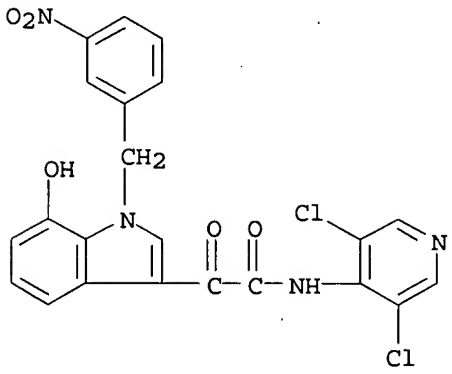
RN 697747-51-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



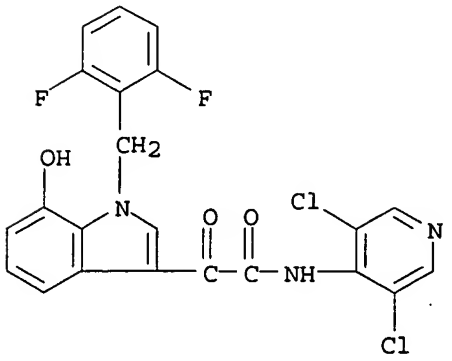
RN 697747-52-7 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2-fluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 697747-53-8 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-1-[(3-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)

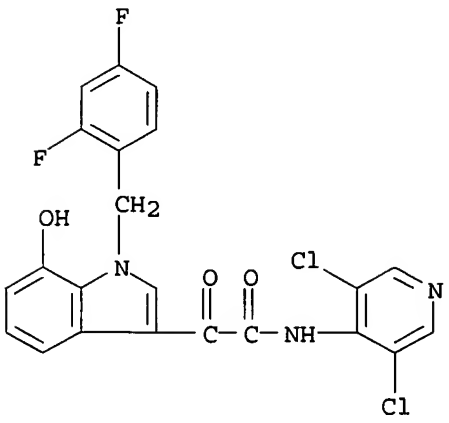


RN 697747-54-9 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

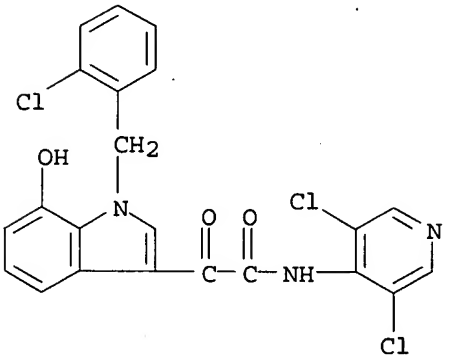


RN 697747-55-0 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,4-

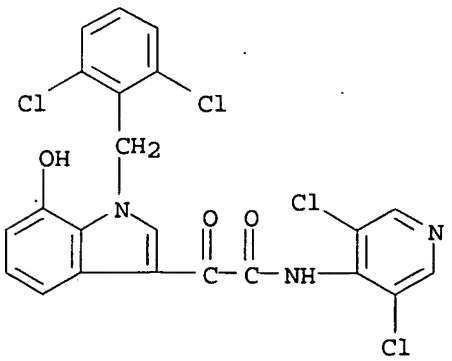
difluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 697747-56-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chlorophenyl)methyl]-N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

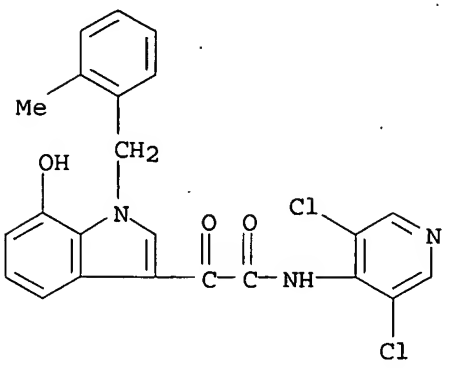


RN 697747-57-2 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2,6-dichlorophenyl)methyl]-N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

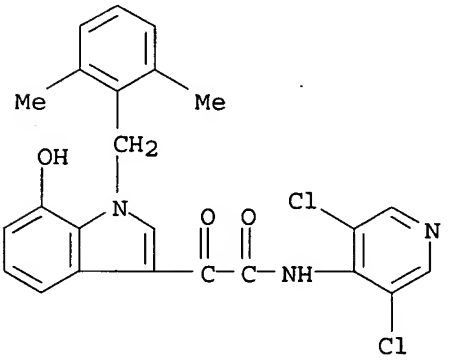


RN 697747-58-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-1-[(2-

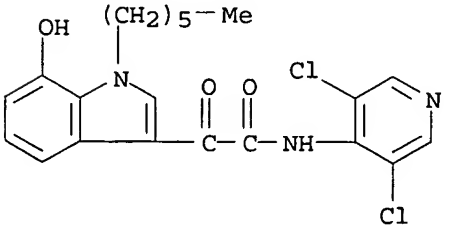
methylphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



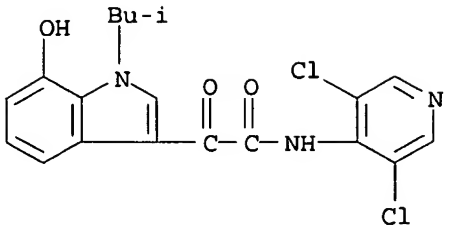
RN 697747-59-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-dimethylphenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



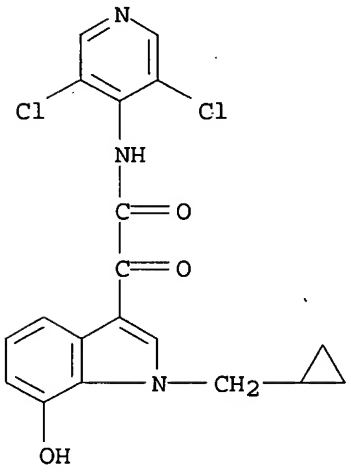
RN 697747-60-7 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-hexyl-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



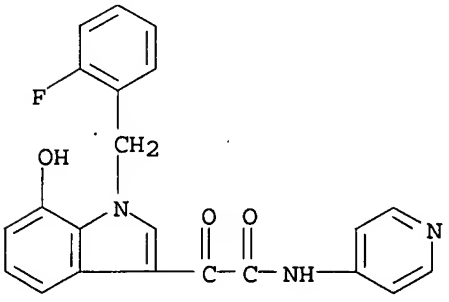
RN 697747-61-8 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-1-(2-methylpropyl)-α-oxo- (9CI) (CA INDEX NAME)



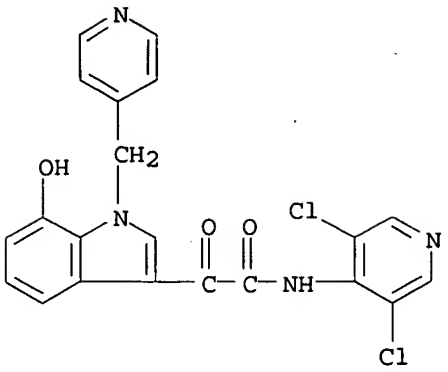
RN 697747-62-9 CAPLUS
CN 1H-Indole-3-acetamide, 1-(cyclopropylmethyl)-N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



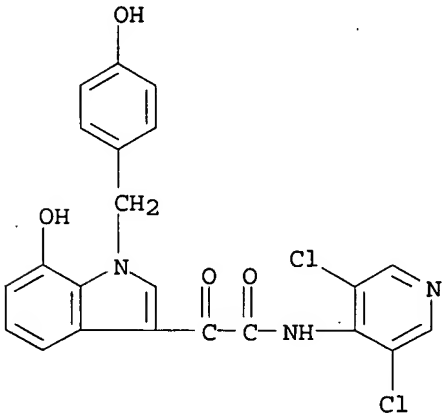
RN 697747-65-2 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-fluorophenyl)methyl]-7-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



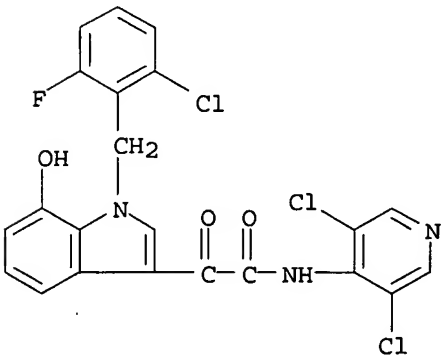
RN 697747-66-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo-1-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



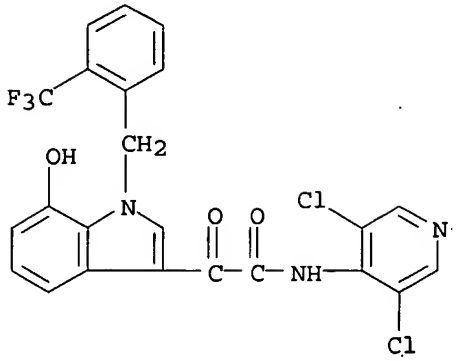
RN 697747-68-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-1-[(4-hydroxyphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



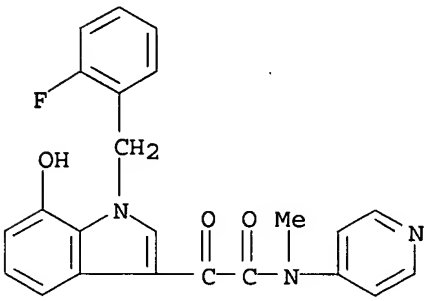
RN 697747-69-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chloro-6-fluorophenyl)methyl]-N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



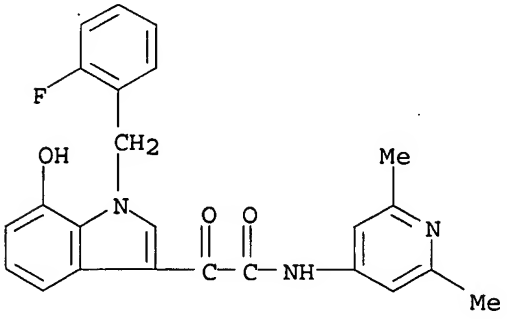
RN 697747-70-9 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-7-hydroxy-α-oxo-1-[[2-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



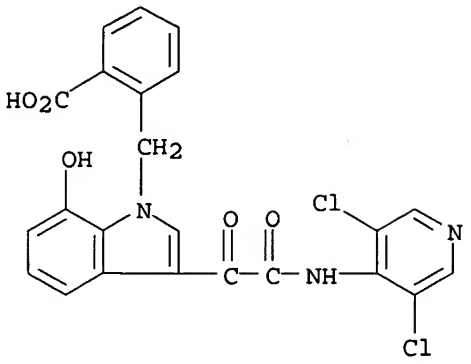
RN 697747-71-0 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-fluorophenyl)methyl]-7-hydroxy-N-methyl-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 697747-72-1 CAPLUS
CN 1H-Indole-3-acetamide, N-(2,6-dimethyl-4-pyridinyl)-1-[(2-fluorophenyl)methyl]-7-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 697747-73-2 CAPLUS
CN Benzoic acid, 2-[[3-[[(3,5-dichloro-4-pyridinyl)amino]oxoacetyl]-7-hydroxy-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:216863 CAPLUS
DOCUMENT NUMBER: 140:247052
TITLE: Treatment nonallergic rhinitis by selective phosphodiesterase 4 inhibitors
INVENTOR(S): Rundfeldt, Chris; Kuss, Hildegard; Hofgen, Norbert
PATENT ASSIGNEE(S): Elbion A.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

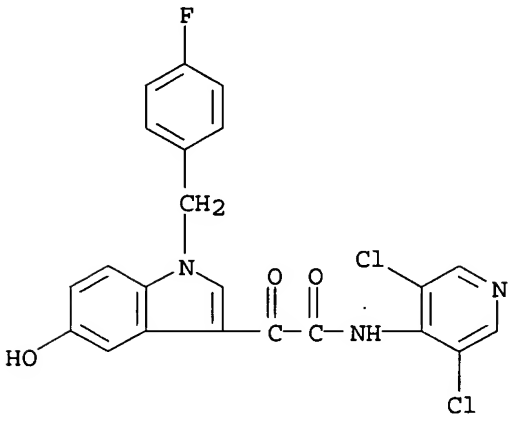
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10241407	A1	20040318	DE 2002-10241407	20020906
US 2004116501	A1	20040617	US 2003-654365	20030903
CA 2497374	AA	20040318	CA 2003-2497374	20030905
WO 2004022041	A2	20040318	WO 2003-EP9895	20030905
WO 2004022041	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1534272	A2	20050601	EP 2003-753390	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014031	A	20050705	BR 2003-14031	20030905
PRIORITY APPLN. INFO.:			DE 2002-10241407	A 20020906
			WO 2003-EP9895	W 20030905

OTHER SOURCE(S): MARPAT 140:247052

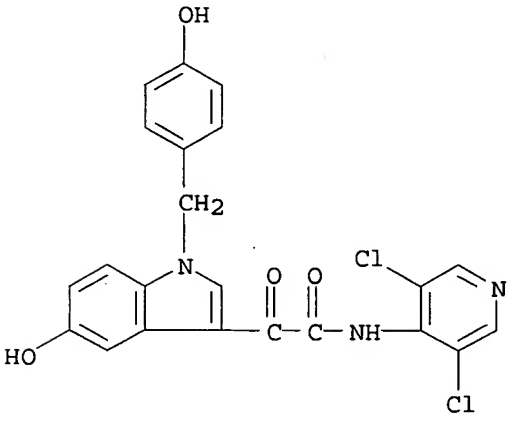
AB The invention discloses the use of hydroxyindolylglyoxylic acid amides as inhibitors of the phosphodiesterase 4 for the treatment of nonallergic rhinitis.

IT **257892-33-4**, AWD 12-281 **671801-82-4**, AWD 12-322
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective phosphodiesterase 4 inhibitors for treatment nonallergic

rhinitis)
RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 671801-82-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-[(4-hydroxyphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:203704 CAPLUS
DOCUMENT NUMBER: 140:229455
TITLE: Combination of glucocorticoids and PDE-4-inhibitors for treating respiratory diseases, allergic diseases, asthma and COPD
INVENTOR(S): Locher, Mathias; Hermann, Robert
PATENT ASSIGNEE(S): Viatris G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

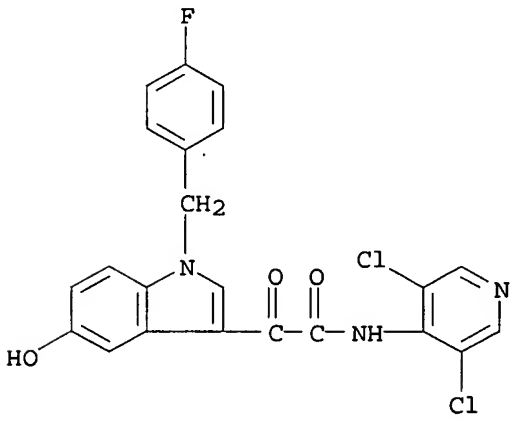
WO 2004019984	A1	20040311	WO 2003-EP8607	20030804
W: AU, BR, CA, CN, CO, CZ, GE, HR, ID, IL, IN, JP, KR, LT, LV, MD, MK, MX, NO, NZ, PL, SG, UA, US, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2492645	AA	20040311	CA 2003-2492645	20030804
EP 1526870	A1	20050504	EP 2003-790851	20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			DE 2002-10236688	A 20020809
			WO 2003-EP8607	W 20030804

AB The invention relates to a novel combination of a glucocorticoid, especially loteprednol, and at least one phosphodiesterase-4 inhibitor (PDE-4-inhibitor), especially hydroxyindole-derivative N-(3,5-dichloropyridine-4-yl)-2-[1-(4-fluorbenzyl)-5-hydroxyindole-3-yl]-2-oxoacetamide, for a simultaneous, sequential or sep. administration in the treatment of respiratory diseases, allergic diseases, asthma and chronic obstructive pulmonary diseases (COPD). Formulation of glucocorticoids and PDE-4-inhibitors can be prepared sep. and applied at the same time or at different times during the day; also combinations can be formulated.

IT **257892-33-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of glucocorticoids and PDE-4-inhibitors for treating respiratory diseases, allergic diseases, asthma and COPD)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:130977 CAPLUS

DOCUMENT NUMBER: 140:281023

TITLE: Anti-inflammatory potential of the selective phosphodiesterase 4 inhibitor N-(3,5-dichloro-pyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxy-indole-3-yl]-glyoxylic acid amide (AWD 12-281), in human cell preparations

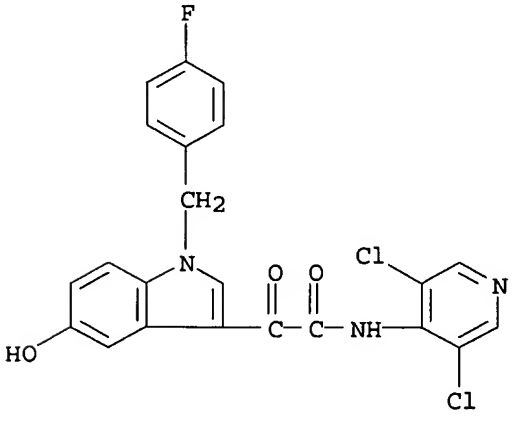
AUTHOR(S): Draheim, Regina; Egerland, Ute; Rundfeldt, Chris

CORPORATE SOURCE: Departments of Pharmacology and Molecular Biology, Elbion AG, Radebeul, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 308(2), 555-563
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AWD 12-281 is a potent (IC50 = 9.7 nM) and highly selective inhibitor of the phosphodiesterase 4 (PDE4) isoenzyme with low affinity to the high-affinity rolipram-binding site. The compound was optimized for topical treatment of asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. The aim of the present study was to assess the effect of AWD 12-281 in human inflammatory cells. Peripheral blood mononuclear cells (PBMCs), diluted whole blood, and human nasal polyp cells derived from surgically resected nasal polyps from patients with polyposis comprise sources of target tissue cells that can be used to predict anti-inflammatory effects in patients. AWD 12-281 was capable of suppressing the production of cytokines in stimulated PBMCs: interleukin-2 (IL-2, phytohemagglutinin stimulation), IL-5 (Con A stimulation), IL-5 and IL-4 (anti-CD3/anti-CD28 co-stimulation), and lipopolysaccharide-stimulated release of tumor necrosis factor α (TNFα). The corresponding values for half-maximum inhibition, EC50, for AWD 12-281 were within a narrow range (46-121 nM). Comparing the effect of AWD 12-281 with roflumilast, cilomilast (SB 207499), rolipram (RPR-73401), and 1-(3-nitrophenyl)-3-(4-pyridylmethyl)pyrido[2,3-d]pyrimidin-2,4(1H,3H)-dione (RS-25344-000), it could be shown that the PDE4 inhibitory activity was closely correlated with inhibitory potential as measured by the above-described assays. AWD 12-281 was also shown to suppress TNFα release in dispersed nasal polyps (EC50 = 111 nM) and in diluted whole blood (EC50 = 934 nM). The reduced activity in human blood may be related to high plasma protein binding. Currently, phase II clin. studies are under way to evaluate the therapeutic potential of AWD 12-281 in asthma, COPD, and allergic rhinitis.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory potential of PDE4 inhibitor AWD 12-281 in human cell prepns.)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

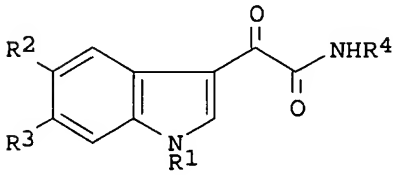


REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:120846 CAPLUS
DOCUMENT NUMBER: 140:163707
TITLE: Method for producing highly pure hydroxyindolylglyoxylic acid amides
INVENTOR(S): Jaensch, Hans-Joachim; Hartenhauer, Helge; Stange, Hans; Hoefgen, Norbert; Schaefer, Juergen
PATENT ASSIGNEE(S): Elbion AG, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013127	A1	20040212	WO 2003-EP8500	20030731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493982	AA	20040212	CA 2003-2493982	20030731
US 2004063939	A1	20040401	US 2003-631475	20030731
EP 1525197	A1	20050427	EP 2003-766389	20030731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013467	A	20050705	BR 2003-13467	20030731

PRIORITY APPLN. INFO.: US 2002-400236P P 20020801
WO 2003-EP8500 W 20030731
OTHER SOURCE(S): CASREACT 140:163707; MARPAT 140:163707
GI



I

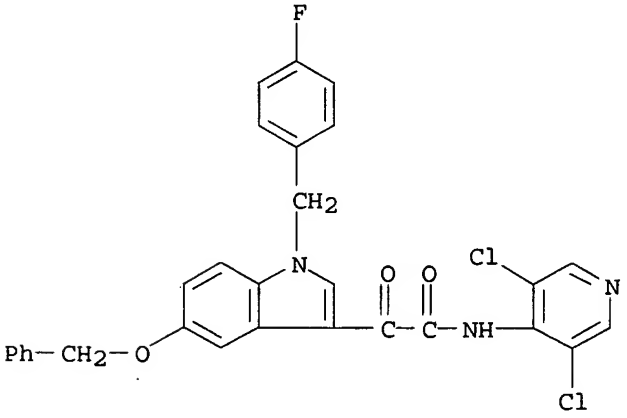
AB The invention relates to a method for producing hydroxyindolylglyoxylic acid amides I [R1 = (un)branched, (un)saturated C1-6-alkyl, 3- to 14-membered mono-, bi- or tricarbocycle, (un)substituted 5- to 15-membered heterocycle (1 - 6 heteroatoms - N, O, S); R2, R3 = H, OH (one or both OH); R4 = (un)substituted mono- or polycyclic aromatic C6-14-carbocycle, 5 to 15-membered heterocycle (containing N, O, S)] in high yields and in a

particularly pure form from 5- or 6-benzyloxyindole or 5,6-di(benzyloxy)indole compds. The method comprises: (a) reaction of 5- or 6-benzyloxyindole or 5,6-di(benzyloxy)indole with R1X (X = halogen); (b) C-acylation of the 1-substituted indole with (COX)2; (c) reaction of the [indol-3-yl]glyoxyl halide with NH3, NH2R4, NH(R4)2; and (d) hydrogenolytic debenzylation. Thus, AWD 12-281 [I; R1 = CH2C6H4F-4, R2 = OH, R3 = H, R4 = 3,5-dichloro-4-pyridyl] was prepared from 5-(benzyloxy)indole via N-benzylation with 4-FC6H4CH2Cl, C-acylation with (COCl)2, amidation with 4-amino-3,5-dichloropyridine, and hydrogenolytic debenzylation of I [R1 = CH2C6H4F-4, R2 = OCH2Ph, R3 = H, R4 = 3,5-dichloro-4-pyridyl].

IT **656237-85-3P**, N-(3,5-Dichloropyrid-4-yl)-[5-(benzyloxy)-1-(4-fluorobenzyl)indol-3-yl]glyoxamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolytic debenzylation of; preparation of highly pure hydroxyindolylglyoxylic acid amides)

RN 656237-85-3 CAPLUS

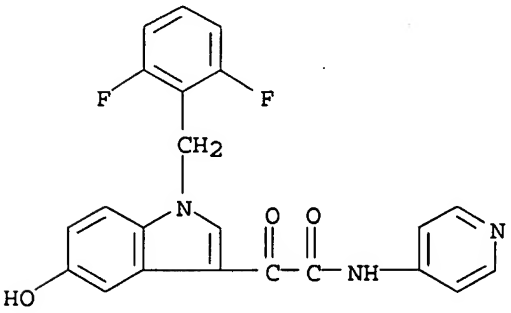
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



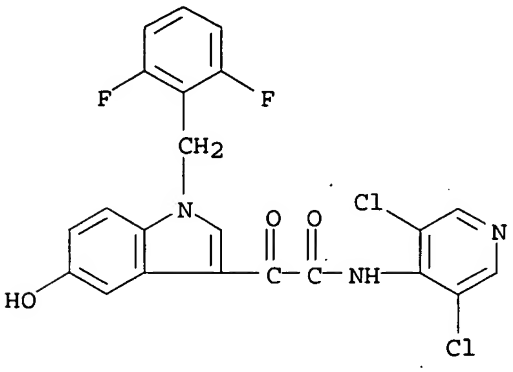
IT **247584-23-2P 247584-24-3P 247584-26-5P 247584-27-6P 247584-28-7P 247584-32-3P 257892-33-4P**, AWD 12-281 **656237-82-0P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of highly pure hydroxyindolylglyoxylic acid amides)

RN 247584-23-2 CAPLUS

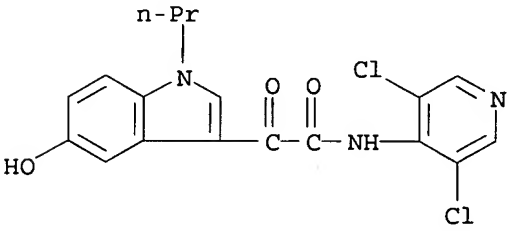
CN 1H-Indole-3-acetamide, 1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



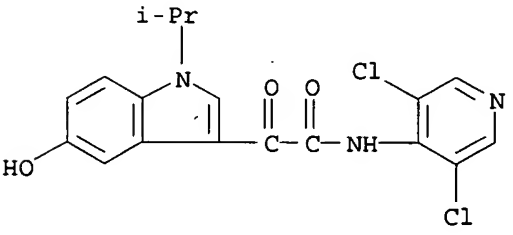
RN 247584-24-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



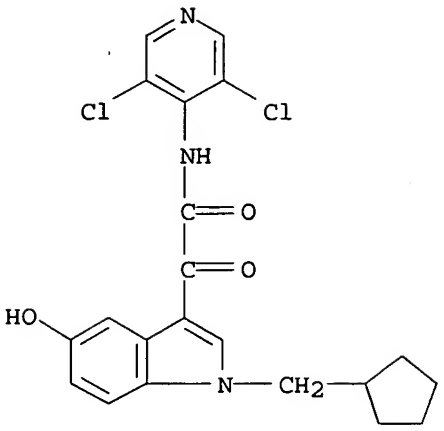
RN 247584-26-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-α-oxo-1-propyl- (9CI) (CA INDEX NAME)



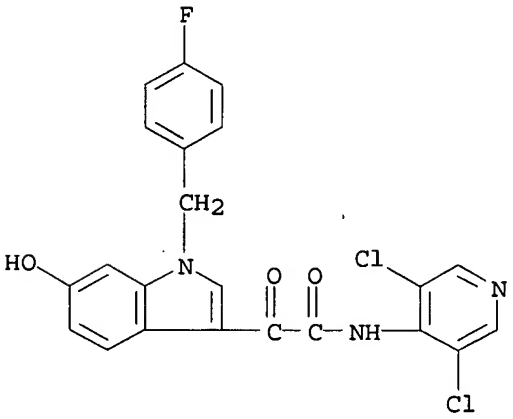
RN 247584-27-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-(1-methylethyl)-α-oxo- (9CI) (CA INDEX NAME)



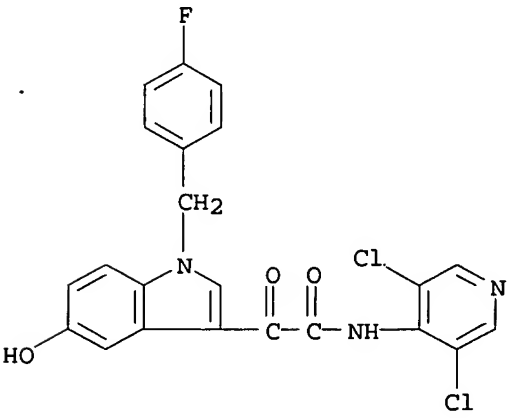
RN 247584-28-7 CAPLUS
CN 1H-Indole-3-acetamide, 1-(cyclopentylmethyl)-N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



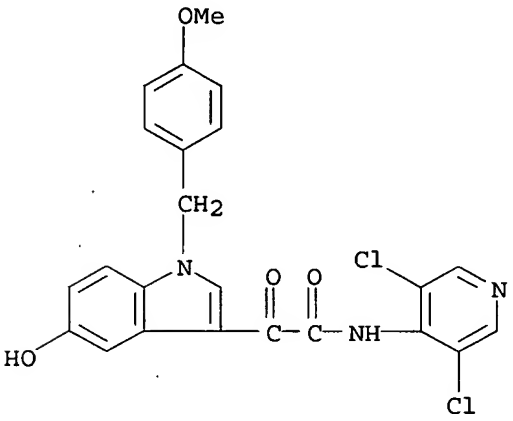
RN 247584-32-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-6-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 656237-82-0 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-[(4-methoxyphenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60309 CAPLUS
DOCUMENT NUMBER: 140:105273
TITLE: Topical treatment of skin diseases
INVENTOR(S): Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann, Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen, Norbert
PATENT ASSIGNEE(S): Elbion AG, Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006920	A1	20040122	WO 2003-EP7514	20030710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004038958	A1	20040226	US 2003-611649	20030701
CA 2492093	AA	20040122	CA 2003-2492093	20030710
BR 2003012696	A	20050426	BR 2003-12696	20030710
EP 1531818	A1	20050525	EP 2003-763810	20030710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
ZA 2005000108	A	20050223	ZA 2005-108	20050106

PRIORITY APPLN. INFO.: US 2002-395221P P 20020711
WO 2003-EP7514 W 20030710

OTHER SOURCE(S): MARPAT 140:105273

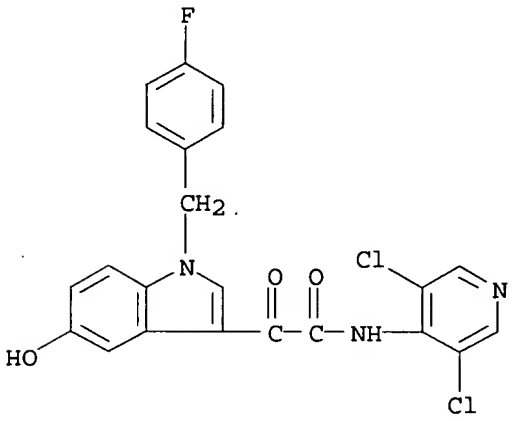
AB The present invention relates to a method for the treatment of an

inflammatory and/or allergic skin disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the topical effectiveness of AWD 12-281 and cilomilast in dermal immunol. inflammation.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitors for treatment of skin inflammatory and/or allergic reactions)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:41257 CAPLUS

DOCUMENT NUMBER: 140:87709

TITLE: Pharmaceutical compositions comprising anticholinergic agents and phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory diseases

INVENTOR(S): Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004704	A1	20040115	WO 2003-EP6668	20030625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10230769	A1	20040122	DE 2002-10230769		20020709
CA 2492026	AA	20040115	CA 2003-2492026		20030625
EP 1521576	A1	20050413	EP 2003-762509		20030625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004058950	A1	20040325	US 2003-614365		20030707
PRIORITY APPLN. INFO.:			DE 2002-10230769	A	20020709
			US 2002-407895P	P	20020903
			WO 2003-EP6668	W	20030625

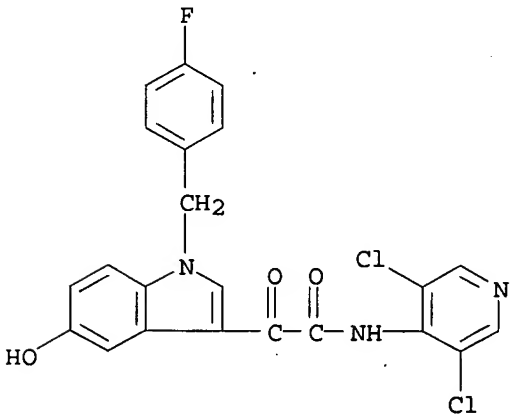
OTHER SOURCE(S): MARPAT 140:87709

AB The invention provides pharmaceutical compns. comprising anticholinergic agents and PDE-IV inhibitors, as well as a method for the production and use thereof in the treatment of respiratory diseases. Powder inhalant formulations are included.

IT **257892-33-4**, AWD-12-281 **645337-16-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising anticholinergic agents and phosphodiesterase IV inhibitors for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



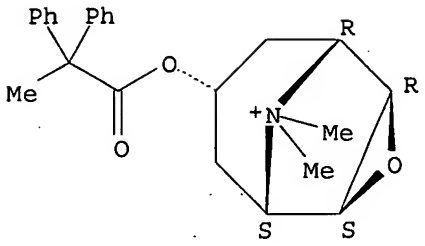
RN 645337-16-2 CAPLUS

CN 3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 9,9-dimethyl-7-(1-oxo-2,2-diphenylpropoxy)-, bromide, (1α,2β,4β,5α,7β)-, mixt. with N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo-1H-indole-3-acetamide (9CI) (CA INDEX NAME)

CM 1

CRN 412046-80-1
CMF C24 H28 N O3 . Br

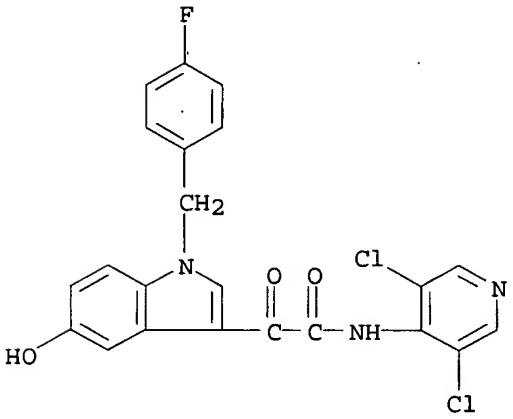
Relative stereochemistry.



● Br^-

CM 2

CRN 257892-33-4
CMF C22 H14 Cl2 F N3 O3



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:913055 CAPLUS
DOCUMENT NUMBER: 139:399770
TITLE: Medical goods comprising heparin or chitosan-based hemocompatible coating
INVENTOR(S): Horres, Roland; Linssen, Marita Katharina; Hoffmann, Michael; Faust, Volker; Hoffmann, Erika; Di Biase, Donato
PATENT ASSIGNEE(S): Hemoteq G.m.b.H., Germany
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094990	A1	20031120	WO 2003-DE1253	20030415

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

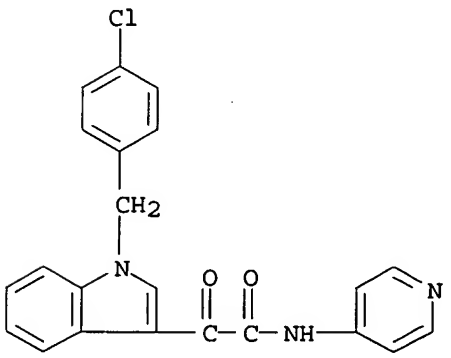
DE 10221055	A1	20031127	DE 2002-10221055	20020510
DE 10261986	A1	20040318	DE 2002-10261986	20020510
CA 2484269	AA	20031120	CA 2003-2484269	20030415
CN 1543362	A	20041103	CN 2003-800770	20030415
EP 1501565	A1	20050202	EP 2003-729829	20030415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011446	A	20050315	BR 2003-11446	20030415
PRIORITY APPLN. INFO.:			US 2002-378676P P	20020509
			DE 2002-10221055 A	20020510
			WO 2003-DE1253 W	20030415

AB The invention relates to oligo- and polysaccharides containing the sugar structural element N-acylglucosamine or N-acylgalactosamine, in addition to the use thereof for producing hemocompatible surfaces and to methods for coating surfaces in a hemocompatible manner with said oligo- and polysaccharides, which constitute the common biosynthetic precursor substances of heparin, heparan sulfates and chitosan. The invention also relates to methods for producing the oligo- and/or polysaccharides, in addition to diverse application options involving hemocompatible surfaces. The invention specifically relates to the use of the oligo- and/or polysaccharides on stents involving at least one hemocompatible coating that has been applied according to the invention and that contains an anti-proliferative, anti-inflammatory and/or athrombogenic active ingredient, to methods for producing said stents and to the use of the latter for preventing restenosis. Thus desulfated and reacetylated heparin was prepared; the Ac-heparin product was used for coating coronary metal stents. The stents were implanted in swines; after four weeks the animals were anesthetized and the artery segments removed for histomorphometric anal.

IT **204205-90-3**, D-24851
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical goods comprising a heparin-based hemocompatible coating)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

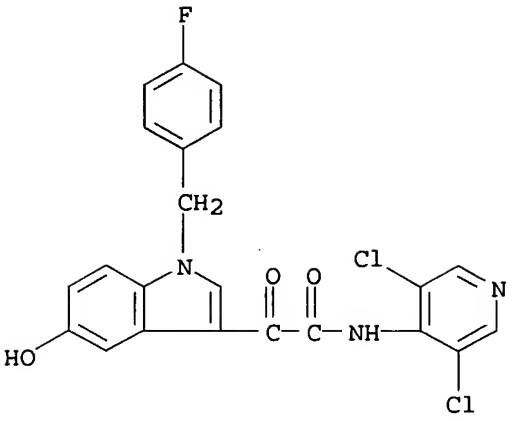
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:775804 CAPLUS
DOCUMENT NUMBER: 140:104940
TITLE: In vivo efficacy in airway disease models of N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide (AWD 12-281), a selective phosphodiesterase 4 inhibitor for inhaled administration
AUTHOR(S): Kuss, H.; Hoefgen, N.; Johanssen, S.; Kronbach, T.; Rundfeldt, C.
CORPORATE SOURCE: Department of Pharmacology, Elbion AG, Radebeul, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 307(1), 373-385
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AWD 12-281 is a highly potent and selective phosphodiesterase 4 (PDE4) inhibitor that was designed to have a metabolic profile that was optimized for topical administration. The aim of the current study was to explore the pharmacol. profile of intratracheally administered AWD 12-281 in different models of asthma and chronic obstructive pulmonary disease (COPD) in comparison with steroids. To assess the anti-inflammatory potential of AWD 12-281, the antigen-induced cell infiltration in bronchoalveolar lavage fluid (BALF) of Brown Norway rats was determined AWD 12-281 (ID50 of 7 μg/kg i.t.) as well as beclomethasone (0.1 μg/kg i.t.) suppresses late-phase eosinophilia when administered intrapulmonary. Furthermore, AWD 12-281 has also strong anti-inflammatory properties when tested in lipopolysaccharide-induced acute lung neutrophilia in Lewis rats (ID50 of 0.02 μg/kg i.t.), ferrets (ID50 of 10 μg/kg i.t.), and domestic pigs (2-4 mg/pig i.t. or 1 mg/kg i.v.). In pigs, AWD 12-281 was as effective as beclomethasone (0.4 mg/pig i.t.) and dexamethasone (0.28 mg/kg i.v.), although at 3 to 10 times the dosage. The bronchodilatory activity of AWD 12-281 was assessed in sensitized guinea pigs. AWD 12-281 (1.5 mg/kg i.t., 1-h pretreatment) inhibited allergen-induced bronchoconstriction by 68% (parameter airway resistance). In sensitized BP-2 mice AWD 12-281 abolished the allergen-induced bronchial hyperresponsiveness and eosinophilia in BALF, showing dose dependence. When given orally, i.v. or i.t., AWD 12-281 has a considerably lower emetic potential than cilomilast in ferrets and roflumilast in pigs. When given topically by inhalation, no emesis could be induced in dogs up to the highest feasible dose (15 mg/kg in 50% lactose blend). These results indicate that AWD 12-281 is a unique potential new drug for the topical treatment of asthma and COPD.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AWD 12-281, a selective phosphodiesterase 4 inhibitor, for inhalation treatment of asthma and chronic obstructive pulmonary disease)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

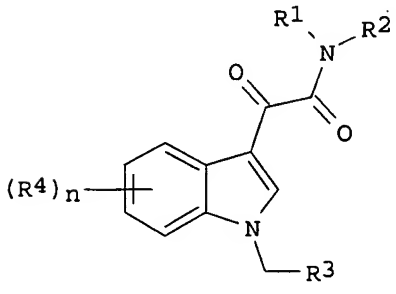


REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:757332 CAPLUS
DOCUMENT NUMBER: 139:276902
TITLE: Preparation of 2-(3-indolyl)-2-oxoacetamide derivatives as angiogenesis inhibitors and anticancer agents
INVENTOR(S): Chen, Chiung-tong; Chen, Shu-jen; Hsu, Ming-chu; Hwang, Der-ren; Li, Wen-tai; Lin, Chu-chung
PATENT ASSIGNEE(S): National Health Research Institutes, Taiwan
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003181482	A1	20030925	US 2002-310711		20021205
US 6903104	B2	20050607			
PRIORITY APPLN. INFO.:			US 2001-337962P	P	20011206

OTHER SOURCE(S): MARPAT 139:276902
GI



I

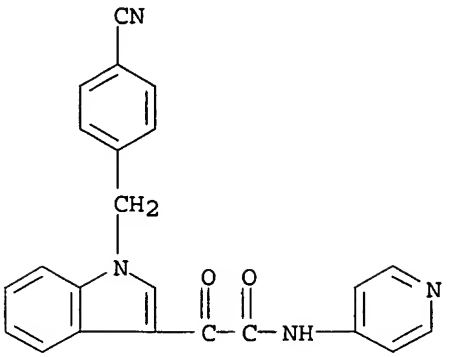
AB This invention relates to novel heteroatom containing compds. [R1 = independently each (un)substituted isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-thiadiazolyl, 1,3-benzothiazolyl, quinolyl, isoquinolyl,

thionaphthenyl, or benzofuranyl; R2 = independently H, each (un)substituted C1-10 alkyl or aryl; or R1 and R2 are taken together with the nitrogen atom to which they are attached to form an (un)substituted 5-8 membered ring comprising C, N, S, or O atoms but not to form 4-phenylpiperazin-1-yl, 4-(pyridin-4-yl)piperazin-1-yl, 4-(pyridin-2-yl)piperazin-1-yl, 4-(2-nitrophenyl)piperazin-1-yl, 4-(3,5-dimethoxyphenyl)piperazin-1-yl, or 4-[bis(4-fluorophenyl)methyl]piperazin-1-yl; R3 = independently each (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl, C4-10 cycloalkenyl, aryl, heteroaryl, or heterocyclyl; R4 = each independently H, NO2, halo, cyano, R7, OR7, CO2R7, SR7, NR7R7, C(O)R7, C(O)NR7R7, OC(O)R7, S(O)2R7, S(O)2NR7R7, NR7C(O)NR7R7, NR7C(O)R7, NR7(CO2R7), NR7S(O)2NR7R7, or NR7S(O)2R7, S(O)2OR7; n = 0, 1, 2, 3, or 4; R7 = independently H, each (un)substituted C1-10 alkyl, C2-10 alkenyl C2-10 alkynyl, C3-10 cycloalkyl, aryl, heteroaryl, or heterocyclyl]. These compds. have potent anticancer, cytotoxic, and anti-angiogenic activity and are useful for the prevention and treatment of diseases, in particular a cancer including a human leukemia, sarcoma, osteosarcoma, lymphoma, melanoma, ovarian, skin, testicular, gastric, pancreatic, renal, breast, prostate colorectal, head and neck, brain, esophageal, bladder, adrenal cortical, lung, bronchus, endometrial, cervical or hepatic cancer, or cancer of unknown primary site. Moreover the cancer is a drug resistance phenotype of which the cancer cells express P-glycoprotein (MDR), multidrug resistance-associated proteins (MRP), lung cancer resistance- associated proteins (LRP), breast cancer resistance proteins (BCRP) or other proteins associated with resistance to anticancer drugs. Thus, a solution of 1.17 g indole 10 mL THF was added dropwise to a suspension of 1.34 g potassium tert-butoxide in 10 mL THF, stirred at room temperature for 2 h, then treated dropwise with a solution of 1.32 g 5-(chloromethyl)-3-methylisoxazole in 5 mL THF, and allowed stand for 4 h, and quenched by adding 10 mL saturated ammonium chloride to give, after workup and silica gel chromatog., 1.61 g 5-(1H-1-indolylmethyl)-3-methylisoxazole (II) (76%). A solution of 212 mg II in 10 mL di-Et ether was added to 254 mg oxalyl chloride dropwise at 0°, stirred at 0° for 3 h, evaporated to remove the solvent, dissolved in 5 mL THF, treated with a solution of 114 mg 3-methyl-5-isothiazolamine and 1 mL Et3N in 10 mL THF dropwise, stirred for 10 h, and then treated with 1 N NaOH (4 mL) to give, after workup and crystallization, 0.27 g I (R1 = 3-methyl-5-isothiazolyl, R2 = R4 = H, R3 = 3-methyl-5-isoxazolyl) (III) (71%). III in vitro inhibited the growth of human cancer cell lines DLD1, HA-22T, HEP G2, HONE1, HR, and NUGC3 with IC50 of 41, 123, 93, 4, 8, and 12 nM, resp.

IT **501921-65-9P**, N-(4-Pyridyl)-2-[1-(4-cyanobenzyl)-1H-indol-3-yl]-2-oxoacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (3-indolyl)oxoacetamide derivs. as angiogenesis inhibitors and anticancer agents)

RN 501921-65-9 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-cyanophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:719308 CAPLUS
DOCUMENT NUMBER: 139:240373
TITLE: Pharmaceutical composition of a phosphodiesterase 4 (PDE4) inhibitor or a PDE3/4 inhibitor and a histamine receptor antagonist for the treatment of respiratory diseases
INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-lutz
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

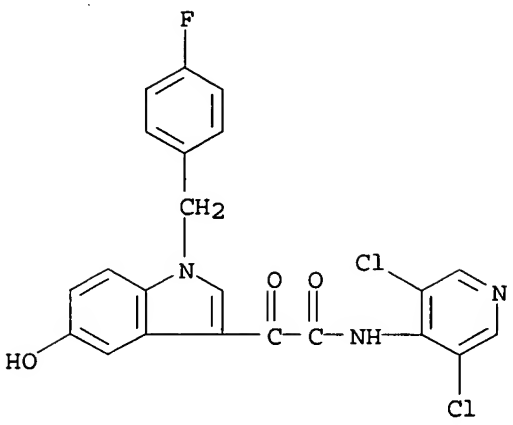
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074055	A1	20030912	WO 2003-EP1876	20030225
W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2478612	AA	20030912	CA 2003-2478612	20030225
EP 1482938	A1	20041208	EP 2003-708130	20030225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008220	A	20050104	BR 2003-8220	20030225
US 2005112069	A1	20050526	US 2003-506875	20030225

PRIORITY APPLN. INFO.: EP 2002-4987 A 20020306
WO 2003-EP1876 W 20030225

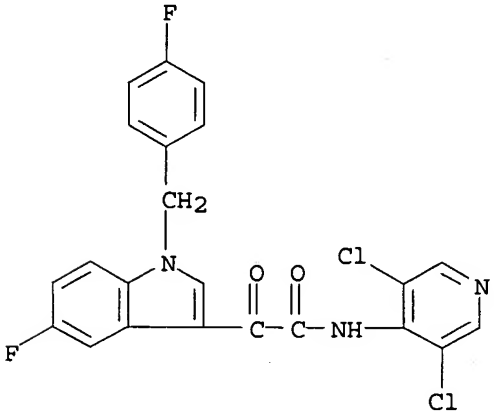
AB The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.

IT **257892-33-4**, AWD 12-281 **444659-44-3**, AWD 12-343
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitor or PDE3/4 inhibitor combination with histamine receptor antagonist for treatment of respiratory disease)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:695438 CAPLUS
DOCUMENT NUMBER: 140:87294
TITLE: AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in the prevention and treatment of inflammatory reactions in a model of allergic dermatitis
AUTHOR(S): Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Rundfeldt, Chris; Kietzmann, Manfred
CORPORATE SOURCE: Department of Pharmacology, Toxicology and Pharmacy, School of Veterinary Medicine, Hannover, D-30559, Germany
SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8), 1107-1114
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal

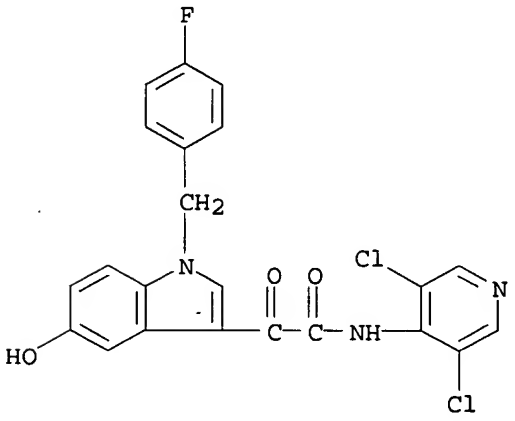
LANGUAGE: English

AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for topical administration, was tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory skin diseases.

IT **257892-33-4**, AWD 12-281
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AWD 12-281, a highly selective phosphodiesterase 4 inhibitor, is effective in prevention and treatment of inflammatory reactions in a model of allergic dermatitis)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376393 CAPLUS

DOCUMENT NUMBER: 138:379220

TITLE: Combination of type 4 phosphodiesterase inhibitor and disease-modifying anti-rheumatic drug for treating rheumatoid arthritis

INVENTOR(S): Barsig, Johannes

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 13 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

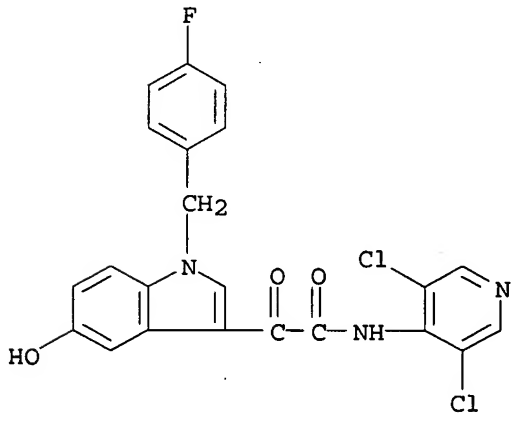
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003092706	A1	20030515	US 2002-184068	20020628
CA 2399840	AA	20030509	CA 2002-2399840	20020827
WO 2003039552	A1	20030515	WO 2002-EP12415	20021107
W: AE, AL, BA, BR, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
EP 1448202	A1	20040825	EP 2002-792742	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508983	T2	20050407	JP 2003-541843	20021107

PRIORITY APPLN. INFO.: EP 2001-607 A 20011109
WO 2002-EP12415 W 20021107

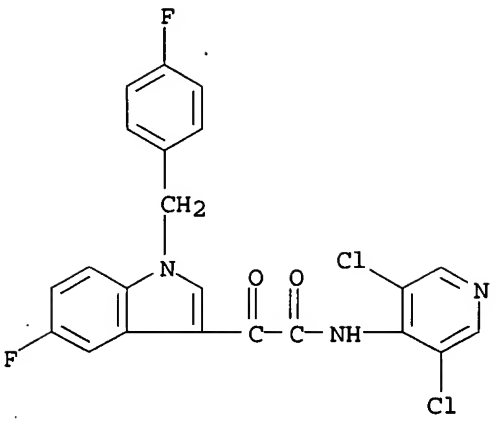
AB The invention relates to the combined administration of a PDE4 or PDE3/4 inhibitor and a disease modifying anti-rheumatic drug (DMARDs) or anti-rheumatic or anti-arthritic drug. Oral treatments with Roflumilast plus methotrexate or Pumafentrine HCl plus methotrexate had additive beneficial effects in delaying the onset and reducing the severity of collagen-induced arthritis in DBA/1 mice.

IT **257892-33-4**, AWD-12-281 **444659-44-3**, AWD 12-343
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDE4 or PDE3/4 inhibitor; combination of phosphodiesterase 4 inhibitor and disease-modifying anti-rheumatic drug for treating rheumatoid arthritis)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)

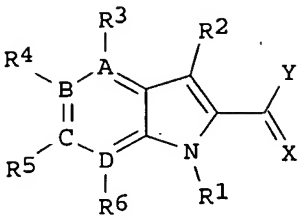


L4 ANSWER 34 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:356415 CAPLUS
DOCUMENT NUMBER: 138:368759
TITLE: Preparation of 2-acylindoles as tubulin polymerization inhibitors for the treatment of metastatic tumors
INVENTOR(S): Beckers, Thomas; Mahboobi, Siavosh; Pongratz, Herwig; Frieser, Markus; Hufsky, Harald; Hockemeyer, Joerg; Vanhoefer, Udo
PATENT ASSIGNEE(S): Baxter Healthcare SA, Switz.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

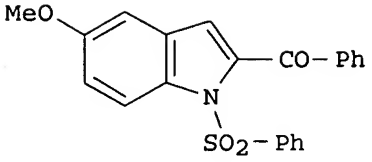
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037861	A1	20030508	WO 2002-EP11883	20021024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10152306	A1	20030724	DE 2001-10152306	20011026
EP 1442015	A1	20040804	EP 2002-802302	20021024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005516895	T2	20050609	JP 2003-540143	20021024

PRIORITY APPLN. INFO.: DE 2001-10152306 A 20011026
WO 2002-EP11883 W 20021024

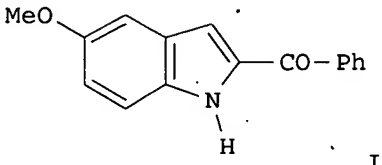
OTHER SOURCE(S): MARPAT 138:368759
GI



I



II



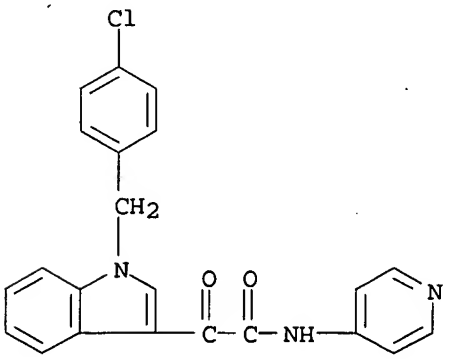
III

AB Title compds. I [R1 = H, alkylcarbonyl, e.g., acetyl, alkyl etc.; R2 = H, halo, CN, etc.; A = B, C, D = independently for a N or C with provisos; Y = electron pair, H, halo with provisos; X = O, S, NH, etc.] and their pharmaceutically acceptable salts were prepared For example, sodium hydroxide mediated deprotection of N-sulfone II, e.g., prepared from benzoyl chloride and 5-methoxy-1-(phenylsulfonyl)-1H-indole, afforded acylindole III. In tubulin polymerization inhibition studies, 8-examples of I exhibited IC50 values ranging from 0.53->10 μM, e.g., the IC50 value of acylindole III was 0.53 μM. Compds. I are claimed useful for the treatment of therapy-resistant and metastatic tumors.

IT **204205-90-3**, D-24851
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of acylindoles as tubulin polymerization inhibitors
for the treatment of metastatic tumors)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242192 CAPLUS
DOCUMENT NUMBER: 138:248511
TITLE: Combination of phosphodiesterase 4 inhibitor and

nonsteroidal antiinflammatory drug in treatment of inflammation

INVENTOR(S): Hatzelmann, Armin; Eltze, Manfrid; Klein, Thomas; Kley, Hans-Peter

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

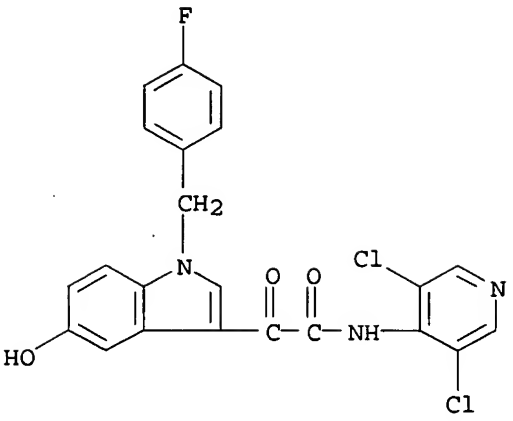
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024489	A2	20030327	WO 2002-EP10424	20020917
WO 2003024489	A3	20030918		
W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
CA 2459757	AA	20030327	CA 2002-2459757	20020917
EP 1429807	A2	20040623	EP 2002-772313	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012606	A	20040817	BR 2002-12606	20020917
JP 2005504077	T2	20050210	JP 2003-528583	20020917
US 2004242597	A1	20041202	US 2004-489920	20040318
ZA 2004002654	A	20050214	ZA 2004-2654	20040405
PRIORITY APPLN. INFO.:			EP 2001-473 A	20010919
			WO 2002-EP10424 W	20020917

AB The invention relates to the combined administration of PDE4-inhibitors and NSAIDs for the treatment of an inflammatory disease and/or an inflammation associated disorder while minimizing gastrointestinal side effects, such as gastric erosions and ulcer, which are frequently associated with the use of NSAIDs. PDE4 inhibitors Rolipram, Roflumilast, and RP73401 inhibited or prevented diclofenac induced gastrointestinal bleeding in mice.

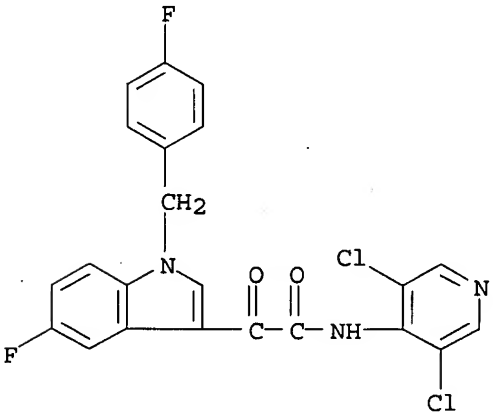
IT **257892-33-4**, AWD 12-281 **444659-44-3**, AWD 12-343
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor; combination of phosphodiesterase 4 inhibitor and nonsteroidal antiinflammatory drug in treatment of inflammation)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 36 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242191 CAPLUS
DOCUMENT NUMBER: 138:248522
TITLE: Combined administration of phosphodiesterase PDE4 or PDE3/4 inhibitors and leukotriene receptor antagonists for the treatment of respiratory tract disorders
INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-Lutz
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024488	A2	20030327	WO 2002-EP10423	20020917
WO 2003024488	A3	20030904		

W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL,

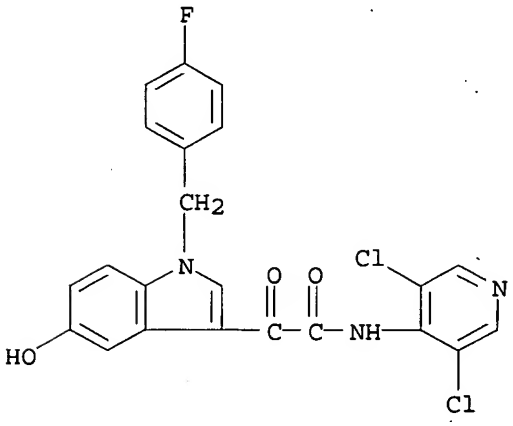
IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, US, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

CA 2460442	AA	20030327	CA 2002-2460442	20020917
EP 1429843	A2	20040623	EP 2002-798730	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012582	A	20041013	BR 2002-12582	20020917
JP 2005505570	T2	20050224	JP 2003-528582	20020917
ZA 2004002653	A	20050214	ZA 2004-2653	20040405
US 2005014762	A1	20050120	US 2004-489903	20040818
PRIORITY APPLN. INFO.:			EP 2001-474 A	20010919
			WO 2002-EP10423 W	20020917

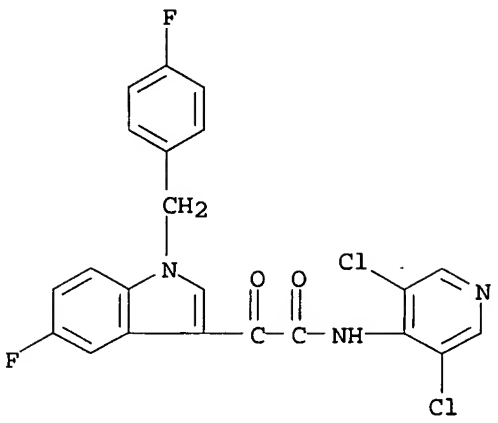
AB The invention relates to the combined administration of PDE4 or PDE3/4 inhibitors and leukotriene receptor antagonists for the treatment of respiratory tract disorders. The inhibitory effects of Roflumilast and Montelukast sodium salt on SRS-A-induced bronchoconstriction were additive in guinea pigs.

IT **257892-33-4 444659-44-3**, AWD 12-343
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor; combined administration of phosphodiesterase PDE4 or PDE3/4 inhibitors and leukotriene receptor antagonists for treatment of respiratory tract disorders)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)

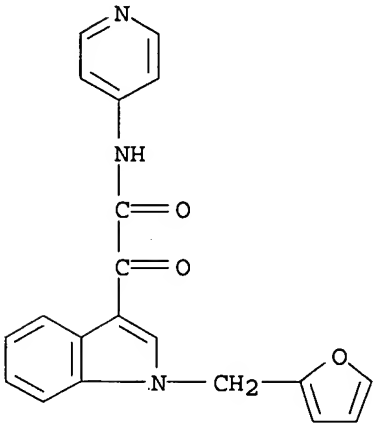


L4 ANSWER 37 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:235682 CAPLUS
DOCUMENT NUMBER: 138:378576
TITLE: Synthesis and Biological Evaluation of N-Heterocyclic Indolyl Glyoxylamides as Orally Active Anticancer Agents
AUTHOR(S): Li, Wen-Tai; Hwang, Der-Ren; Chen, Ching-Ping; Shen, Chien-Wei; Huang, Chen-Long; Chen, Tung-Wei; Lin, Chi-Hung; Chang, Yee-Ling; Chang, Ying-Ying; Lo, Yue-Kan; Tseng, Huan-Yi; Lin, Chu-Chung; Song, Jeng-Shin; Chen, Hua-Chien; Chen, Shu-Jen; Wu, Se-Hui; Chen, Chiung-Tong
CORPORATE SOURCE: Division of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Taipei, 114, Taiwan
SOURCE: Journal of Medicinal Chemistry (2003), 46(9), 1706-1715
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:378576

AB A series of N-heterocyclic indolyl glyoxylamides were synthesized and evaluated for in vitro and in vivo anticancer activities. They exhibited a broad spectrum of anticancer activity not only in murine leukemic cancer cells but also in human gastric, breast, and uterus cancer cells as well as their multidrug resistant sublines with a wide range of IC50 values. They also induced apoptosis and caused DNA fragmentation in human gastric cancer cells. Among the compds. studied, N1-(3-Methyl-5-isothiazolyl)-2-1-[(3-methyl-5-isoxazolyl)methyl]-1H-3-indolyl-2-oxoacetamide (I) showed the most potent activity of growth inhibition (IC50 = 17-1711 nM) in several human cancer cells. Given orally, compds. I and N1-(3-Methyl-5-isothiazolyl)-2-[1-(4-cyanobenzyl)-1H-3-indolyl]-2-oxoacetamide dose-dependently prolonged the survival of animals inoculated with P388 leukemic cancer cells. N-Heterocyclic indolyl glyoxylamides may be useful as orally active chemotherapeutic agents against cancer and refractory cancerous diseases of multidrug resistance phenotype.

IT **528593-64-8P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. evaluation of N-Heterocyclic indolyl glyoxylamides as orally active anticancer agents in relation to apoptosis induction

and partition coefficient)
RN 528593-64-8 CAPLUS
CN 1H-Indole-3-acetamide, 1-(2-furanylmethyl)-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

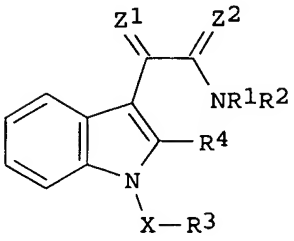
L4 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:221515 CAPLUS
DOCUMENT NUMBER: 138:238008
TITLE: Preparation of 3-glyoxlylamide indoles as anticancer agents useful against multidrug-resistant cancer cells
INVENTOR(S): Koya, Keizo; Sun, Lijun; Ono, Mitsunori; Liang, Guiqing; James, David; Li, Hao; Xia, Zhi-Qiang
PATENT ASSIGNEE(S): SBR Pharmaceuticals Corp., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022280	A2	20030320	WO 2002-US27513	20020828
WO 2003022280	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2460347	AA	20030320	CA 2002-2460347	20020828
EP 1427416	A2	20040616	EP 2002-757457	20020828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504790	T2	20050217	JP 2003-526409	20020828
US 2003092751	A1	20030515	US 2002-232394	20020829
PRIORITY APPLN. INFO.:			US 2001-322022P	P 20010913

WO 2002-US27513 W 20020828

OTHER SOURCE(S): MARPAT 138:238008

GI



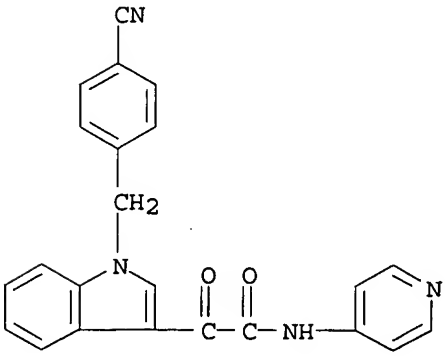
I

AB The anti-cancer compound has a structural formula I wherein Z1 and Z2 are independently O, S, NOR5 or NR5, and R1-R5 are H, aliphatic group, aryl group or other specifically defined groups. Thus, 2-(1-(4-chloro-benzyl)-1-indo-3-yl)-N-(3-methyl-isothiazol-5-yl)-2-oxo-acetamide was prepared from oxylyl chloride 5.1 mmol,1-(4'-chlorobenzyl)-indole (4.14 mmol) and 5-amino-3-methylisothiazole (9.73 mmol), and demonstrated significantly high anti-cancer activity (IC50 0.0005 μM) against five cancer lines with wide variety of multidrug-resistant cancer cell types (MDA 435, HL 60, DU 146, MES SA, and H2).

IT **501921-65-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of glyoxylamide indoles as anticancer agents useful against multidrug-resistant cancer cells)

RN 501921-65-9 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-cyanophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 39 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:5806 CAPLUS

DOCUMENT NUMBER: 138:78456

TITLE: Composition comprising a PDE-4 inhibitor and H1-receptor antagonist for treatment of respiratory diseases

INVENTOR(S): Knowles, Richard Graham; Ward, Peter; Nials, Anthony Terence

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

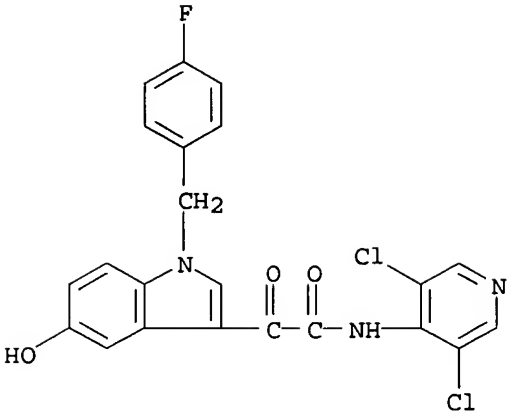
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000289	A1	20030103	WO 2002-GB2679	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450758	AA	20030103	CA 2002-2450758	20020617
EP 1404369	A1	20040407	EP 2002-735611	20020617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1518460	A	20040804	CN 2002-812473	20020617
BR 2002010473	A	20040810	BR 2002-10473	20020617
JP 2005501023	T2	20050113	JP 2003-506932	20020617
US 2004176419	A1	20040909	US 2003-480969	20031208
ZA 2003009587	A	20050117	ZA 2003-9587	20031210
PRIORITY APPLN. INFO.:			GB 2001-15181 A	20010620
			WO 2002-GB2679 W	20020617

AB A method of prophylaxis, treating, or reducing the duration or frequency of the exacerbations associated with a respiratory disease, such as chronic obstructive pulmonary disease or asthma, comprises administering to a patient an effective amount of a phosphodiesterase-4 (PDE-4) inhibitor, e.g., cilomilastat, in combination with an H1-receptor antagonist, e.g., loratadine. For example, a metered dose inhaler (e.g., for 120 actuations) was prepared containing cilomilast 18 mg, loratadine 12 mg, and 1,1,1,2-tetrafluoroethane to 75.0 mg.

IT **257892-33-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising PDE-4 inhibitor and H1-receptor antagonist for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:965129 CAPLUS
DOCUMENT NUMBER: 138:44711
TITLE: Pharmaceutical compositions based on anticholinergics and PDE-IV inhibitors
INVENTOR(S): Pairet, Michel; Meade, Christopher J. M.; Pieper, Michael P.
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Provisional Ser. No. 281,857.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002193393	A1	20021219	US 2002-93240	20020307
DE 10110772	A1	20020912	DE 2001-10110772	20010307
US 2004024007	A1	20040205	US 2003-613783	20030703
US 2005148562	A1	20050707	US 2004-6940	20041208

PRIORITY APPLN. INFO.:

DE 2001-10110772	A	20010307
US 2001-281857P	P	20010405
DE 2000-10054042	A	20001031
US 2000-253613P	P	20001128
DE 2000-10062712	A	20001215
DE 2000-10063957	A	20001220
US 2000-257220P	P	20001221
US 2000-257221P	P	20001221
DE 2001-10111058	A	20010308
DE 2001-10113366	A	20010320
US 2001-281653P	P	20010405
US 2001-281874P	P	20010405
DE 2001-10138272	A	20010810
US 2001-314599P	P	20010824
US 2001-7182	B1	20011019
US 2001-86145	B1	20011019
US 2001-27662	B1	20011220
DE 2002-10206505	A	20020216
US 2002-92116	A1	20020306

US 2002-93240	B1	20020307
US 2002-100659	A1	20020318
US 2002-369213P	P	20020401
US 2003-360064	A2	20030207
US 2003-413065	B2	20030414
US 2003-419358	A1	20030421
US 2003-613783	A2	20030703
US 2004-763894	A2	20040123
US 2004-775901	A2	20040210
US 2004-776757	A2	20040211
US 2004-824391	A2	20040414

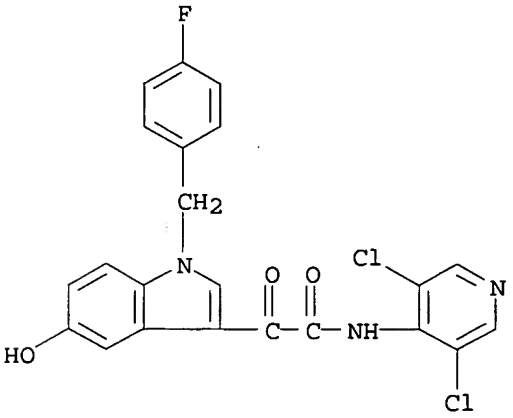
OTHER SOURCE(S): MARPAT 138:44711

AB The present invention relates to novel pharmaceutical compns. based on anticholinergics and phosphodiesterase (PDE) IV inhibitors, processes for preparing them and their use in the treatment of respiratory tract diseases. For example, a suspension aerosol contained tiotropium bromide 0.029%, AWD 12-281 0.033%, ethanol 0.5%, iso-Pr myristate 0.1%, and TG 227 to 100%.

IT **257892-33-4**, AWD 12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation compns. based on anticholinergics and phosphodiesterase IV inhibitors for treatment of respiratory tract diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 41 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:695761 CAPLUS

DOCUMENT NUMBER: 137:237718

TITLE: Inhalant compositions containing anticholinergics and PDE IV inhibitors

INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael Paul

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069945	A2	20020912	WO 2002-EP1988	20020226

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     WO 2002069945        A3    20030130
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     DE 10110772          A1    20020912   DE 2001-10110772      20010307
     CA 2439763           AA    20020912   CA 2002-2439763       20020226
     EP 1372649           A2    20040102   EP 2002-727329        20020226
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004521134        T2    20040715   JP 2002-569122        20020226
     BR 2002007883        A     20040727   BR 2002-7883          20020226
     NZ 528621            A     20050429   NZ 2002-528621        20020226
     ZA 2003006221        A     20040722   ZA 2003-6221          20030812
PRIORITY APPLN. INFO.:                     DE 2001-10110772   A  20010307
                                           WO 2002-EP1988     W  20020226
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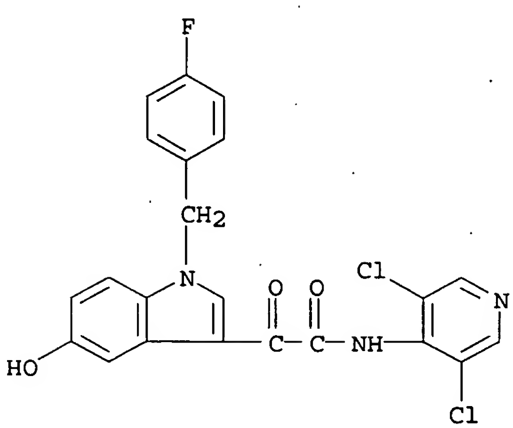
OTHER SOURCE(S): MARPAT 137:237718

AB The invention relates to drug compns. based on anticholinergics and PDE IV inhibitors, to methods for their production, and to their use as inhalants for the treatment of respiratory tract diseases. Thus an inhalation powder was composed of capsules that contained (μg/capsule): tiotropium bromide 21.7; AWD-12-281 200; lactose 4778.3.

IT **257892-33-4**, AWD-12-281
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhalant compns. containing anticholinergics and PDE IV inhibitors)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 42 OF 61 CAPLUS

ACCESSION NUMBER: 2002:575737 CAPLUS

DOCUMENT NUMBER: 137:135500

TITLE: Methods of inducing ovulation by administering a non-polypeptide cAMP level modulator

INVENTOR(S): Palmer, Stephen; McKenna, Sean; Tepper, Mark; Eshkol,

Aliza; MacNamee, Michael C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 928,268.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

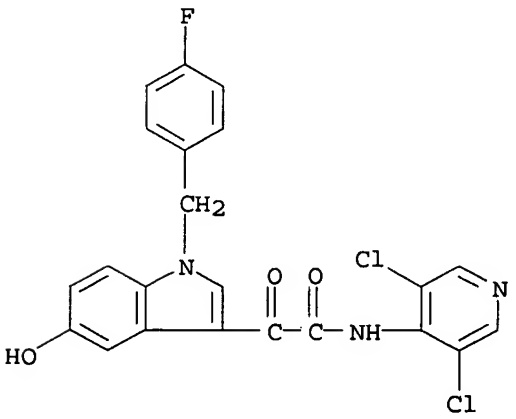
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103106	A1	20020801	US 2001-14812	20011214
US 2002065324	A1	20020530	US 2001-928268	20010810
CA 2469939	AA	20030626	CA 2001-2469939	20011214
EP 1463493	A1	20041006	EP 2001-274987	20011214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017198	A	20041026	BR 2001-17198	20011214
JP 2005516924	T2	20050609	JP 2003-552277	20011214
US 2005148501	A1	20050707	US 2003-498639	20011214

PRIORITY APPLN. INFO.: US 2000-224962P P 20000811
US 2001-928268 A2 20010810
WO 2001-EP14730 W 20011214

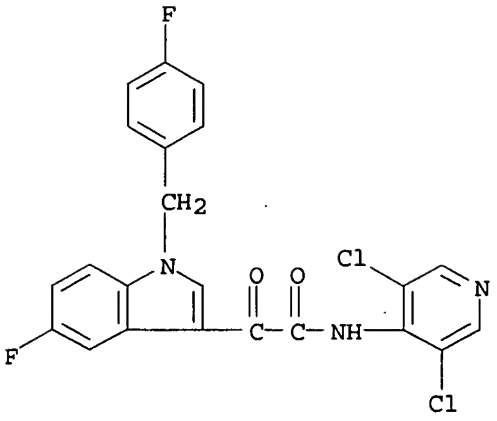
AB The present invention relates to methods of inducing ovulation in a female host comprising the administration of a non-polypeptide cAMP level modulator to the female host. In another aspect, the invention provides for specific administration of the phosphodiesterase inhibitor prior to the luteal phase of the host's ovulatory cycle. Preferred non-polypeptide cAMP level modulator include phosphodiesterase inhibitors, particularly inhibitors of phosphodiesterase 4 isoforms. Pharmaceutical compns. containing the cAMP modulators are also claimed.

IT **257892-33-4**, AWD-12-281 **444659-44-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of inducing ovulation by administering a non-polypeptide cAMP level modulator)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 444659-44-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



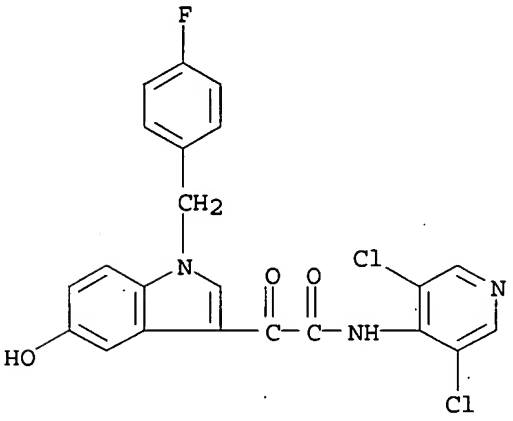
L4 ANSWER 43 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:495906 CAPLUS
DOCUMENT NUMBER: 138:117605
TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic dermatitis
AUTHOR(S): Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Ehinger, Britt; Kietzmann, Manfred
CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany
SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear skin) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB'207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.

IT **257892-33-4**, AWD 12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on inflammatory reaction in a model of allergic dermatitis)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

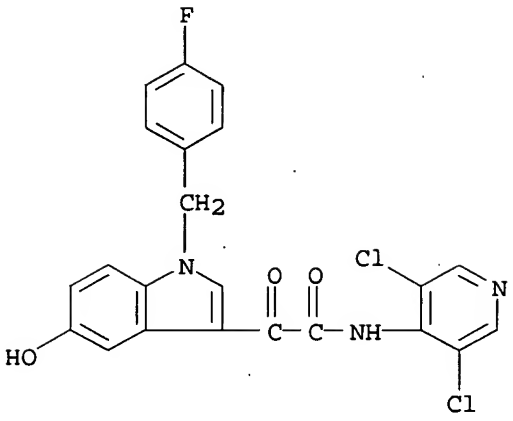


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:420229 CAPLUS
DOCUMENT NUMBER: 138:18980
TITLE: AWD 12-281
AUTHOR(S): Kuss, H.; Hofgen, N.; Egerland, U.; Heer, S.; Marx, D.; Szelenyi, I.; Schupke, H.; Gasparic, A.; Olbrich, M.; Hempel, R.; Hartenhauer, H.; Krone, D.; Berthold, K.; Kronbach, T.; Rundfeldt, C.
CORPORATE SOURCE: Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany
SOURCE: Drugs of the Future (2002), 27(2), 111-116
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Airway diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases whose prevalence is increasing. Current research concerned with developing effective treatments for these conditions have focused on the search for alternatives to the standard corticosteroid antiinflammatory therapy. Selective phosphodiesterase 4 (PDE4) inhibitors have received a considerable amount of attention due to their ability to suppress the functions of several cell types involved in allergic and inflammatory disorders. The selective PDE4 inhibitor AWD 12-281 is the result of a pharmacophore-based synthesis program wherein the optimization process was supported by ligand-based drug design methods. AWD 12-281 was selected for further development for its high affinity and selectivity for the human PDE4 isoenzyme and due to its potent activity and excellent tolerability in models of allergic rhinitis, asthma and COPD, especially after topical treatment.

IT **257892-33-4P**, AWD 12-281
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(AWD 12-281: preparation, pharmacodynamics, pharmacokinetics, and toxicity)
RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

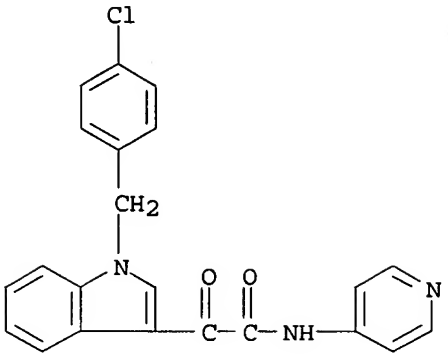


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:915607 CAPLUS
DOCUMENT NUMBER: 136:193482
TITLE: New small-molecule tubulin inhibitors
AUTHOR(S): Bacher, G.; Beckers, T.; Emig, P.; Klenner, T.; Kutschert, B.; Nickel, B.
CORPORATE SOURCE: IUPAC Commission, Research & Development Oncology, ASTA Medica AG, Frankfurt, 60314, Germany
SOURCE: Pure and Applied Chemistry (2001), 73(9), 1459-1464
CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER: International Union of Pure and Applied Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The variety of biol. agents directed toward the tubulin system exceeds those acting on DNA, making it an important target for cancer chemotherapy. However. the complicated chemical structures and restricted access to the natural resources, in combination with the development of drug resistance, limit the first generation of natural products. Considerable efforts in the search and synthesis of new synthetic compds., such as small mol. tubulin inhibitors, gave access to novel potential/promising drugs. Among these substances, two series of novel, easily accessible indole classes were identified as tubulin-destabilizing agents. Owing to the synthetic nature, potent in vitro and in vivo antitumoral activity, and efficacy against multidrug-resistant (MDR) tumors, D-24851 and D-64131 have significant potential in cancer treatment.

IT **204205-90-3**, D-24851
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small-mol. tubulin inhibitors)
RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

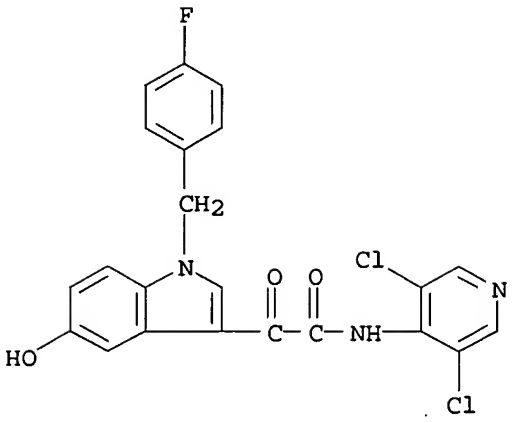
L4 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:850920 CAPLUS
DOCUMENT NUMBER: 135:366766
TITLE: Method for enhancing cognitive function with phosphodiesterase-4 inhibitors
INVENTOR(S): Hagan, James
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001087281	A2	20011122	WO 2001-GB2134		20010515
WO 2001087281	A3	20020328			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1292287	A2	20030319	EP 2001-929824		20010515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003533473	T2	20031111	JP 2001-583749		20010515
US 2003187006	A1	20031002	US 2003-275853		20030314
PRIORITY APPLN. INFO.:			GB 2000-11802	A	20000516
			WO 2001-GB2134	W	20010515

AB A method for enhancing cognitive function by administering to a patient in need thereof an effective amount of a PDE4 inhibitor.

IT **257892-33-4**, AWD-12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancing cognitive function with phosphodiesterase-4 inhibitors)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

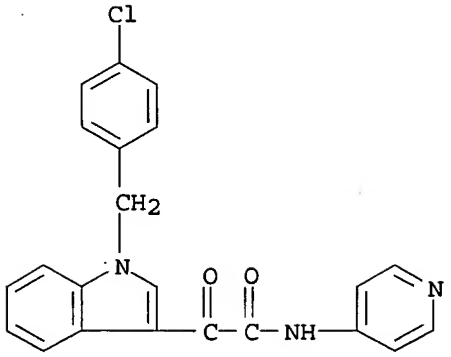


L4 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:790429 CAPLUS
DOCUMENT NUMBER: 136:200078
TITLE: Synthesis and characterization of the biologically active 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide
AUTHOR(S): Knaack, Martin; Emig, Peter; Bats, Jan W.; Kiesel, Michael; Muller, Arndt; Gunther, Eckhard
CORPORATE SOURCE: Infracor GmbH, Hanau, 63457, Germany
SOURCE: European Journal of Organic Chemistry (2001), (20), 3843-3847
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:200078

AB The spectroscopic characterization of the new potent tubulin inhibitor 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide (D-24851), which is under preclin. development, is described. The synthesis was optimized and follows a straightforward route from the unsubstituted indole via 1-(4-chlorobenzyl)indole and 1-[(4-chlorophenyl)methyl]-α,-oxo-N-4-pyridinyl-1H-indole-3-acetyl chloride to the target compound, D-24851. The structure was assigned by sophisticated NMR expts., for example a 1,1-ADEQUATE experiment, and X-ray crystallog.

IT **204205-90-3P**, D-24851
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and characterization of 1-[(4-chlorophenyl)methyl]-α-oxo-N-(4-pyridinyl)acetamide (D-24851))

RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:783704 CAPLUS
DOCUMENT NUMBER: 136:112307
TITLE: Differential roles of p21Waf1 and p27Kip1 in modulating chemosensitivity and their possible application in drug discovery studies
AUTHOR(S): Schmidt, Mathias; Lu, Yang; Parant, John M.; Lozano, Guillermina; Bacher, Gerald; Beckers, Thomas; Fan, Zhen
CORPORATE SOURCE: Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Molecular Pharmacology (2001), 60(5), 900-906
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

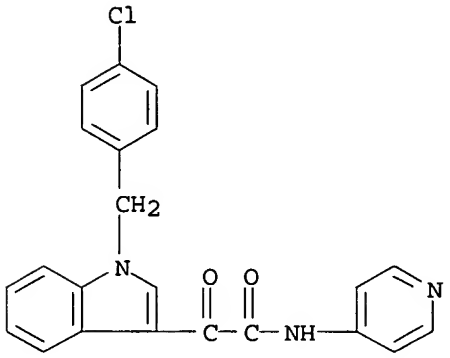
AB In this study, the differential role of the cyclin-dependent kinase (CDK) inhibitors p21Waf1 and p27Kip1 in cell cycle regulation was proposed for use in screening natural or synthetic compds. for cell cycle-dependent (particularly M phase-dependent) antineoplastic activity. P21Waf1 or p27Kip1 was ectopically expressed with an ecdysone-inducible mammalian expression system in a human colon adenocarcinoma cell line. Induction of p21Waf1 or p27Kip1 expression inhibited the activities of CDK2 and completely arrested cells at G1 phase of the cell cycle by p27Kip1 and at G1 and G2 phases by p21Waf1. We examined the sensitivity of these cells to several antineoplastic agents known to be cell cycle-dependent or -independent. Substantially increased resistance to cell cycle-dependent antineoplastic agents was found in the cells when the expression of p21Waf1 or p27Kip1 was induced. In contrast, only a desensitization to cell cycle-independent antineoplastic agents was found in the cells arrested by p21Waf1 or p27Kip1. Because p21Waf1 induces an addnl. block at G2 phase that inhibits cell entry into M phase, we further examined the difference between p21Waf1- and p27Kip1-induced cells in their sensitivity to D-24851, a novel M phase-dependent compound We found that induction of p21Waf1 after exposure of the cells to D-24851 conferred stronger resistance than did induction of p27Kip1. Taken together, our results suggest that the differential effect of p21Waf1 and p27Kip1 on cell cycle regulation may be advantageous for screening chemical libraries for novel antineoplastic candidates that are cell cycle-dependent, and M phase-dependent in particular.

IT **204205-90-3**, D 24851
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(differential roles of p21Waf1 and p27Kip1 in modulating chemosensitivity and possible application in drug discovery studies)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 49 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:467995 CAPLUS

DOCUMENT NUMBER: 135:46111

TITLE: Preparation of N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamides as antitumor agents

INVENTOR(S): Guenther, Eckhard; Emig, Peter; Reichert, Dietmar; Le Baut, Guillaume; Nickel, Bernd; Bacher, Gerald

PATENT ASSIGNEE(S): Asta Medica A.-G., Germany

SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

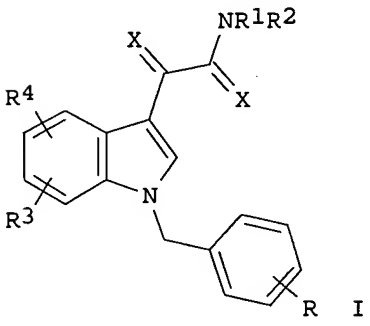
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19962300	A1	20010628	DE 1999-19962300	19991223
US 2001014690	A1	20010816	US 2000-736431	20001215
US 6432987	B2	20020813		
CA 2395259	AA	20010705	CA 2000-2395259	20001219
WO 2001047913	A2	20010705	WO 2000-EP12947	20001219
W: AT, AU, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
BR 2000016712	A	20020903	BR 2000-16712	20001219
EP 1240157	A2	20020918	EP 2000-983349	20001219
EP 1240157	B1	20040211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
JP 2003519137	T2	20030617	JP 2001-549383	20001219
AT 259364	E	20040215	AT 2000-983349	20001219
AU 772745	B2	20040506	AU 2001-20119	20001219

PT 1240157	T	20040630	PT 2000-983349		20001219
NZ 519977	A	20040827	NZ 2000-519977		20001219
ES 2215768	T3	20041016	ES 2000-983349		20001219
NZ 533731	A	20050324	NZ 2000-533731		20001219
ZA 2002004896	A	20021220	ZA 2002-4896		20020619
NO 2002003039	A	20020809	NO 2002-3039		20020621
BG 106924	A	20030430	BG 2002-106924		20020716
PRIORITY APPLN. INFO.:			DE 1999-19962300	A	19991223
			WO 2000-EP12947	W	20001219

OTHER SOURCE(S): MARPAT 135:46111

GI



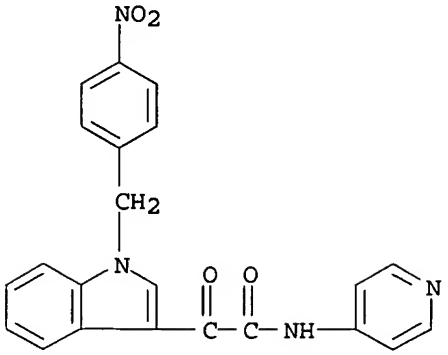
I

AB Title compds. [I; R1 = H, (substituted) alkyl, benzyloxycarbonyl, t-butoxycarbonyl, OAc; R2 = (substituted) Ph, pyridinyl, pyrimidinyl, etc.; or R1R2 = (substituted) (homo)piperazinyl; R3, R4 = H, alkyl, cycloalkyl, alkanoyl, alkoxy, halo, PhCH2O, NO2, amino, etc.; R = NO2, amino, (di)alkylamino, cycloalkylamino, phenylalkylamino, (hetero)aroylamino, etc.; X = O, S] were prepared as antitumor agents (no data). Thus, (COCl)2 in Et2O at 0° was treated dropwise with indole in Et2O and refluxed for 3 h followed by dropwise addition of 4-aminopyridine in THF at 5° and reflux over night to give 43.3% N-(pyridin-4-yl) (indol-3-yl)glyoxylamide. The product was treated with 4-nitrobenzyl chloride to give 64% N-(pyridin-4-yl) [1-(4-nitrobenzyl)indol-3-yl]glyoxylamide (D-68836). The latter was subjected to catalytic hydrogenation to give 94% N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamide (D-68838). D-68838 was said to inhibit polymerization of tubulin.

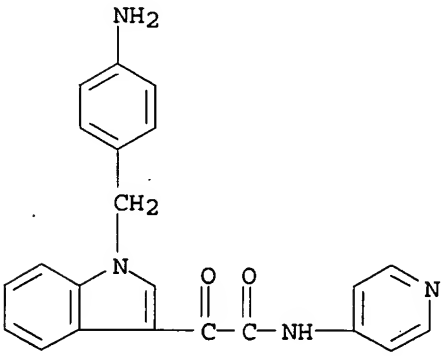
IT **344799-93-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridinyl aminobenzylindolylglyoxylamides as antitumor agents)

RN 344799-93-5 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-nitrophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



IT **344799-91-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyl aminobenzylindolylglyoxylamides as antitumor agents)
RN 344799-91-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-aminophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:380415 CAPLUS
DOCUMENT NUMBER: 134:361385
TITLE: Combined phosphodiesterase 3 (PDE3) and phosphodiesterase 4 (PDE4) inhibitor therapy for the treatment of obesity
INVENTOR(S): Snyder, Peter
PATENT ASSIGNEE(S): Icos Corporation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035979	A2	20010525	WO 2000-US42137	20001113
WO 2001035979	A3	20020103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

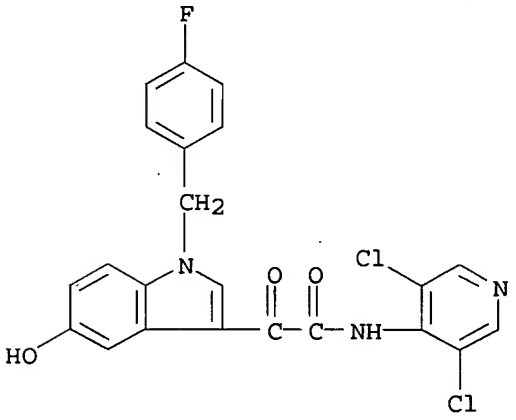
PRIORITY APPLN. INFO.: US 1999-165418P P 19991113

AB Materials and methods are provided for the treatment of obesity that involve a combination of a PDE3 and PDE4 inhibitor in synergistically effective amts. Methods for producing PDE proteins are also described.

IT **257892-33-4**, AWD-12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 3 and phosphodiesterase 4 inhibitor combination therapy for treatment of obesity)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:260010 CAPLUS

DOCUMENT NUMBER: 135:86768

TITLE: Requirement of additional adenylate cyclase activation for the inhibition of human eosinophil degranulation by phosphodiesterase IV inhibitors

AUTHOR(S): Ezeamuzie, C. I.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Faculty of Medicine, P.O. Box 24923, Kuwait University, Safat, 13110, Kuwait

SOURCE: European Journal of Pharmacology (2001), 417(1/2), 11-18
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

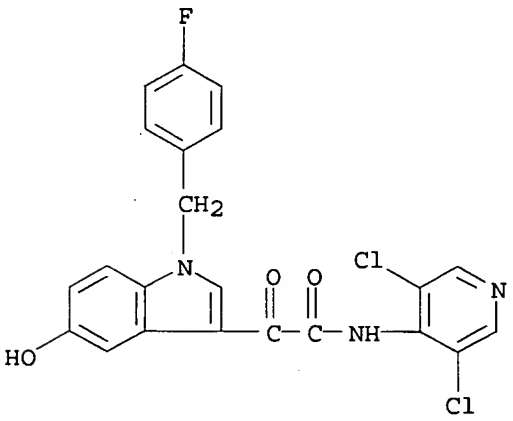
AB Human eosinophils contain predominantly phosphodiesterase type IV, but selective inhibitors of this isoenzyme fail to inhibit certain eosinophil responses such as degranulation. In this study, the effect of activation of adenylate cyclase on the ability of several highly selective PDE IV

inhibitors to inhibit complement C5a-induced O2- release and degranulation of human eosinophils in vitro was investigated. All four selective PDE IV inhibitors, N-(3,5-dichloropyrid-4-yl)-3-cyclopentyl-oxy-4-methoxybenzamide (RP 73401), rolipram, N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxy-indol-3-yl]glyoxylacidamide (AWD 12-281) and c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl-r-1-cyclohexane carboxylic acid) (SB 207499) potently inhibited C5a-induced O2- generation (IC50=0.03, 0.42, 0.55 and 0.86 μM, resp.), but generally failed to inhibit degranulation. The only exception was AWD 12-281, which inhibited degranulation (IC50=16.2 μM). In the presence of different AC activators (histamine, salbutamol, prostaglandin E2 and forskolin), the PDE IV inhibitors became potent inhibitors of degranulation. The interaction between the PDE IV inhibitors and the AC activators resulted in a synergistic increase in intracellular levels of adenosine 3', 5'-monophosphate (cAMP). These results show that PDE IV inhibitors generally require an addnl. cAMP signal to be able to inhibit eosinophil degranulation, and that this signal can be generated via both membrane receptors and direct AC activation. This may be relevant to the in vivo effectiveness of PDE IV inhibitors in eosinophilic inflammation.

IT **257892-33-4**, AWD 12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(requirement of addnl. adenylate cyclase activation for inhibition of human eosinophil degranulation by phosphodiesterase IV inhibitors)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:259980 CAPLUS

DOCUMENT NUMBER: 135:57779

TITLE: Identification of inhibitor binding sites of the cAMP-specific phosphodiesterase 4

AUTHOR(S): Richter, W.; Unciuleac, L.; Hermsdorf, T.; Kronbach, T.; Dettmer, D.

CORPORATE SOURCE: Medical Faculty, Institute of Biochemistry, University of Leipzig, Leipzig, D-04103, Germany

SOURCE: Cellular Signalling (2001), 13(4), 287-297
CODEN: CESIEY; ISSN: 0898-6568

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

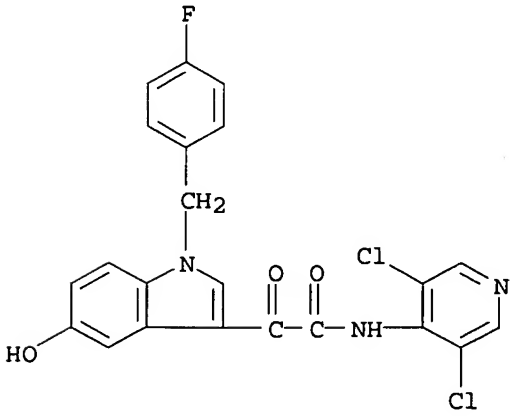
LANGUAGE: English

AB Using the technique of site-directed mutagenesis, point mutants of human PDE4A have been developed in order to identify amino acids involved in inhibitor binding. Relevant amino acids were selected according to a peptidic binding site model for PDE4 inhibitors, which suggests interaction with two tryptophan residues, one histidine and one tyrosine residue, as well as one Zn2+ ion. Mutations were directed at those tryptophan, histidine, and tyrosine residues, which are conserved among the PDE4 subtypes (PDE4A-D) and lie within the high-affinity 4-[3-(cyclopentoxyl)-4-methoxyphenyl]-2-pyrrolidone (rolipram) binding domain of human PDE4A (amino acids 276-681 according to the PDE4A sequence L20965). Truncations to this region do not alter enzyme activity or inhibitor sensitivity. The mutants were expressed in COS1 cells, and the recombinant cyclic nucleotide phosphodiesterase (PDE) forms have been characterized in terms of their catalytic activity and inhibitor sensitivities. Tyrosine residues 432 and 602, as well as histidine 588, were found to be involved in inhibitor binding, but no interaction was detected between tryptophan and PDE inhibitors tested. To test the possibility that other amino acids are of importance for hydrophobic interactions, selected phenylalanine residues were also mutated. We found phenylalanine 613 and 645 to influence inhibitor binding to PDE4. The significant differences in the inhibitor sensitivities of the mutants show that the various inhibitors have different enzyme binding sites. Based on the assumption that the known side effects of PDE4 inhibitors (like emesis and nausea) are caused directly by selective inhibition of different conformation states of PDE4, our results may be a hint to differ between PDE4 inhibitors, which have emetic side effects (like rolipram), and those that do not have side effects (like N-(3,5-dichlorpyrid-4-yl)-[1-(4-fluorbenzyl)-5-hydroxy-indol-3-yl]-glyoxylateamide [AWD12-281]) by the differences of their binding sites and in that context contribute to the development of novel drugs. Furthermore, the identification of amino acid interactions proposed by the peptidic binding site model, which was used for the mutant selection, verifies the PrGen modeling as a useful method for the prediction of inhibitor binding sites in cases where detailed knowledge of the protein structure is not available.

IT **257892-33-4**, AWD12-281
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(identification of inhibitor binding sites of cAMP-specific phosphodiesterase 4)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:247170 CAPLUS
DOCUMENT NUMBER: 134:261240
TITLE: Indolyl-3-glyoxylic acid derivatives comprising therapeutically valuable properties
INVENTOR(S): Nickel, Bernd; Klenner, Thomas; Bacher, Gerald; Beckers, Thomas; Emig, Peter; Engel, Juergen; Bruyneel, Erik; Kamp, Guenter; Peters, Kirsten
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022954	A2	20010405	WO 2000-EP9390	20000926
WO 2001022954	A3	20020328		
W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19946301	A1	20010419	DE 1999-19946301	19990928
US 2003114511	A1	20030619	US 2000-492531	20000127
US 6693119	B2	20040217		
CA 2386069	AA	20010405	CA 2000-2386069	20000926
EP 1218006	A2	20020703	EP 2000-967789	20000926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510274	T2	20030318	JP 2001-526166	20000926
EE 200200169	A	20030415	EE 2002-169	20000926
BR 2000014378	A	20030729	BR 2000-14378	20000926
NZ 517988	A	20041029	NZ 2000-517988	20000926
NO 2002001367	A	20020522	NO 2002-1367	20020319
ZA 2002002556	A	20030704	ZA 2002-2556	20020402
BG 106639	A	20021229	BG 2002-106639	20020423
US 2004171668	A1	20040902	US 2003-686809	20031017

PRIORITY APPLN. INFO.:

DE 1999-19946301	A	19990928
DE 1998-19814838	A	19980402
US 1999-285058	A2	19990402
US 2000-492531	A1	20000127
WO 2000-EP9390	W	20000926

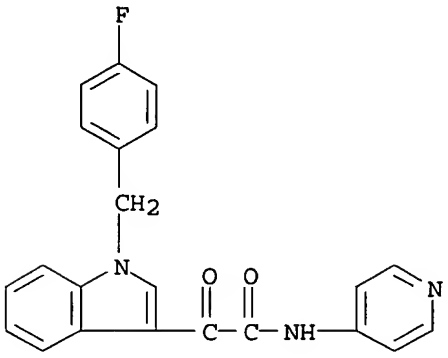
OTHER SOURCE(S): MARPAT 134:261240

AB The invention relates to the use of N-substituted indol-3- glyoxylamides of for treating tumors, in particular, in cases of drug resistance and metastatic carcinoma, and as angiogenesis inhibitors having distinctly fewer side effects, in particular, distinctly lower neurotoxicity. The invention also relates to medicaments containing the inventive compds.

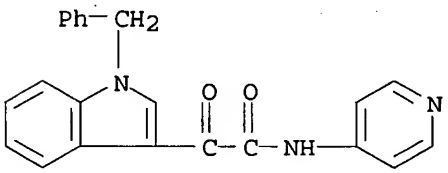
IT **204205-78-7**, D 24241 **204205-86-7**, D 24843
204205-90-3, D 24851 **245661-47-6**, D 25505
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indolyl-3-glyoxylic acid derivs. comprising therapeutically valuable properties)

RN 204205-78-7 CAPLUS

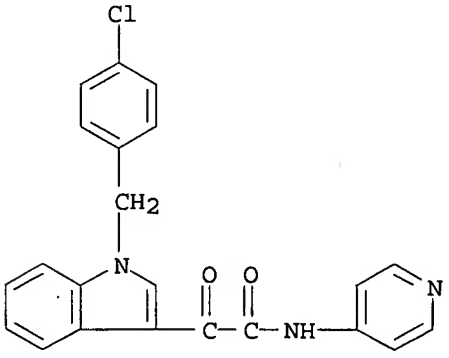
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



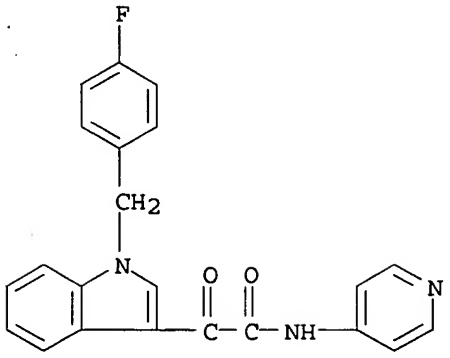
RN 204205-86-7 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-1-(phenylmethyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 245661-47-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:58000 CAPLUS
DOCUMENT NUMBER: 134:290069
TITLE: D-24851, a novel synthetic microtubule inhibitor, exerts curative antitumoral activity in vivo, shows efficacy toward multidrug-resistant tumor cells, and lacks neurotoxicity
AUTHOR(S): Bacher, Gerald; Nickel, Bernd; Emig, Peter; Vanhoefer, Udo; Seeber, Siegfried; Shandra, Alexei; Klenner, Thomas; Beckers, Thomas
CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt am Main, 60314, Germany
SOURCE: Cancer Research (2001), 61(1), 392-399
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

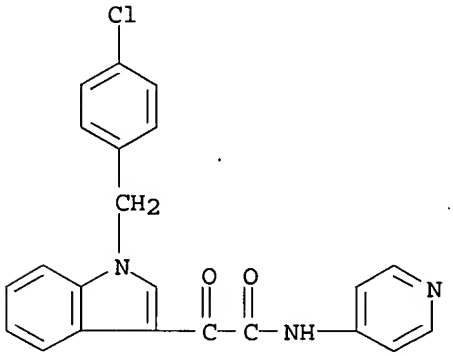
AB N-(pyridin-4-yl)-[1-(4-chlorbenzyl)indol-3-yl]glyoxylamide (D-24851) is a novel synthetic compound that was identified in a cell-based screening assay to discover cytotoxic drugs. D-24851 destabilizes microtubules and blocks cell cycle transition specifically at G2-M phase. The binding site of D-24851 does not overlap with the tubulin binding sites of known microtubule-destabilizing agents like vincristine or colchicine. In vitro, D-24851 has potent cytotoxic activity toward a panel of established human tumor cell lines including SKOV3 ovarian cancer, U87 glioblastoma, and ASPC-1 pancreatic cancer cells. In vivo, oral D-24851 treatment induced complete tumor regressions (cures) in rats bearing Yoshida AH13 sarcomas. Of importance is that the administration of curative doses of D-24851 to the animals revealed no systemic toxicity in terms of body weight loss and neurotoxicity in contrast to the administration of paclitaxel or vincristine. Interestingly, multidrug-resistant cell lines generated by vincristine-driven selection or transfection with the Mr 170,000 P-glycoprotein encoding cDNA were rendered resistant toward paclitaxel, vincristine, or doxorubicin but not towards D-24851 when compared with the parental cells. Because of its synthetic nature, its oral applicability, its potent in vitro and in vivo antitumoral activity, its efficacy against multidrug-resistant tumors, and the lack of neurotoxicity, D-24851 may have significant potential for the treatment of various malignancies.

IT **204205-90-3**, D 24851
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(D-24851, a novel synthetic microtubule inhibitor, exerts curative antitumoral activity in vivo, shows efficacy toward multidrug-resistant tumor cells, and lacks neurotoxicity)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:30560 CAPLUS

DOCUMENT NUMBER: 134:221365

TITLE: The effect of selective and non-selective phosphodiesterase inhibitors on allergen- and leukotriene C4-induced contractions in passively sensitized human airways

AUTHOR(S): Schmidt, Dunja T.; Watson, Nikki; Dent, Gordon; Ruhlmann, Elke; Branscheid, Detlev; Magnussen, Helgo; Rabe, Klaus F.

CORPORATE SOURCE: Department of Pulmonology, Leiden University Medical Centre, Leiden, NL-2333 ZA, Neth.

SOURCE: British Journal of Pharmacology (2000), 131(8), 1607-1618
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

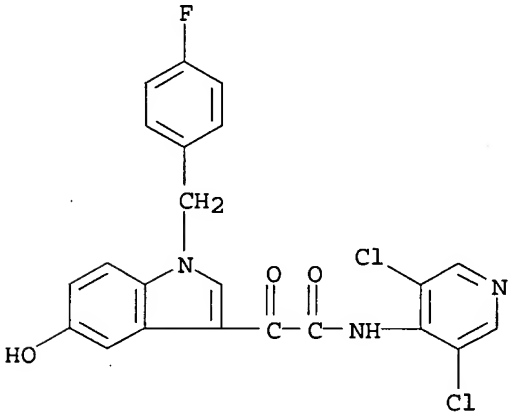
AB Non-selective inhibitors of cyclic nucleotide phosphodiesterase (PDE) block allergen-induced contraction of passively sensitized human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of histamine and cysteinyl leukotriene (LT) release from airways. We investigated the effects of non-selective PDE inhibitors and selective inhibitors of PDE3 and PDE4 in order to determine the involvement of PDE isoenzymes in the suppression of allergic bronchoconstriction. Macroscopically normal airways from 76 patients were sensitized with IgE-rich sera (>250 u ml-1) containing specific antibodies against allergen (Dermatophagoides farinae). Contractile responses of bronchial rings were assessed using standard organ bath techniques. Passive sensitization caused increased contractile responses to allergen, histamine and LTC4. Non-selective PDE inhibitors (theophylline, 3-isobutyl-1-methylxanthine [IBMX]), a PDE3-selective inhibitor (motapizone), PDE4-selective inhibitors (RP73401, rolipram, AWD 12-281) and a mixed PDE3/4 inhibitor (zardaverine) all significantly relaxed inherent bronchial tone at resting tension and to a similar degree. Theophylline, IBMX, zardaverine and the combination of motapizone and RP73401 inhibited the contractile responses

to allergen and LTC4. Pre-treatment with motapizone, RP73401, rolipram or the methylxanthine adenosine receptor antagonist, 8-phenyltheophylline, did not significantly decrease responses to either allergen or LTC4. We conclude that combined inhibition of PDE3 and PDE4, but not selective inhibition of either isoenzyme or antagonism of adenosine receptors, is effective in suppressing allergen-induced contractions of passively sensitized human airways. The relationship between allergen- and LTC4-induced responses suggests that PDE inhibitors with PDE3 and PDE4 selectivity are likely to act in part through inhibition of mediator release and not simply through direct relaxant actions on airway smooth muscle.

IT **257892-33-4**, AWD 12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphodiesterase inhibitors in allergen- and leukotriene C4-induced contractions in sensitized human airways)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

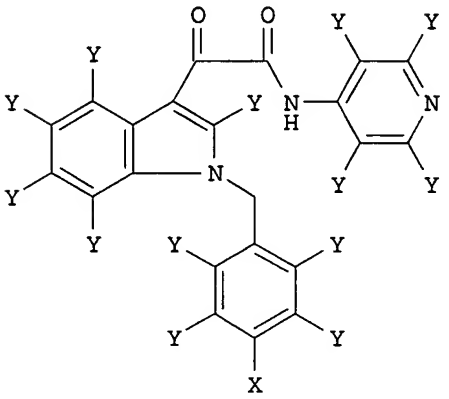
L4 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:814353 CAPLUS
DOCUMENT NUMBER: 133:359224
TITLE: Fatty acid-N-substituted indol-3-glyoxylamide compositions as antitumor agents
INVENTOR(S): Bradley, Matthews O.; Swindell, Charles S.; Anthony, Forrest; Webb, Nigel L.; Fisher, Mark
PATENT ASSIGNEE(S): Protarga, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067802	A1	20001116	WO 2000-US12752	20000510

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-133292P P 19990510
OTHER SOURCE(S): MARPAT 133:359224
GI



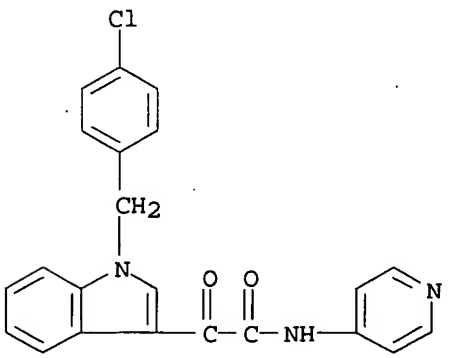
I

AB The present invention pertains to N-substituted indol-3-glyoxylamides that are conjugates of fatty acids and conjugates of I. The conjugates are useful in treating cancer. In an example taxoprexin completely eliminated all measureable tumors in 7 out of 8 mice at 120 mg/kg/day for 5 days while paclitaxel retarded tumor growth for about 4 days.

IT **204205-90-3D**, conjugates, with antitumor agents
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty acid-N-substituted indol-3-glyoxylamide compns. as antitumor agents)

RN 204205-90-3 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



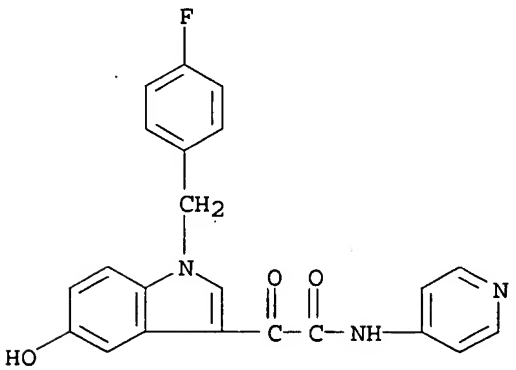
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:55462 CAPLUS
DOCUMENT NUMBER: 132:202635
TITLE: A peptidic binding site model for PDE 4 inhibitors
AUTHOR(S): Polymeropoulos, Emmanuel E.; Hofgen, Norbert
CORPORATE SOURCE: Department of Chemical Research, Corporate R and D ASTA Medica Group, Frankfurt, D-60314, Germany
SOURCE: Quantitative Structure-Activity Relationships (1999), 18(6), 543-547
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

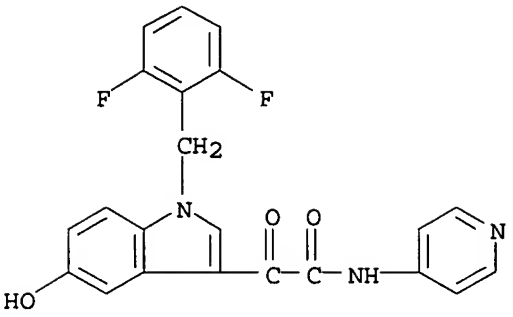
AB The pseudoreceptor modeling program PrGen was used to construct a peptidic binding site model for phosphodiesterase 4 inhibitors. A training set of 21 diverse compds. (rolipram, nitraquazone and xanthine derivs., imidazo pyrido pyrazinones and 5-oxyindoles) was used to construct the binding site surrogate consisting of five amino acid residues, a Zn+2 cofactor and an envelope of charged virtual particles. The model was validated by predicting the free energies of binding ΔGpred0 of ten ligands (rolipram, imidazo pyrido pyrazinones and 5-oxyindoles). In seven cases the prediction was satisfactory. The rms deviation [4] in ΔG0 is 0.16 and 1.82 kcal/mol-resulting in an uncertainty in IC50 (or Ki) of 1.32 and 22.81-for the training and the test set resp., while the corresponding maximal prediction errors in ΔGpred0 were 0.27 kcal/mol and 4.50 kcal/mol.

IT **204206-02-0 247584-23-2 247584-24-3**
247584-27-6 247584-34-5 257892-33-4
260265-54-1 260265-55-2 260265-56-3
260265-57-4 260265-58-5 260265-59-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptidic binding site model for PDE 4 inhibitors)

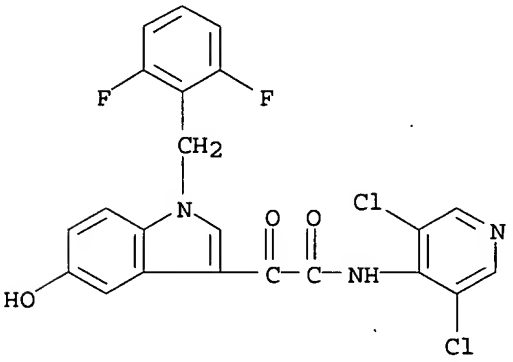
RN 204206-02-0 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



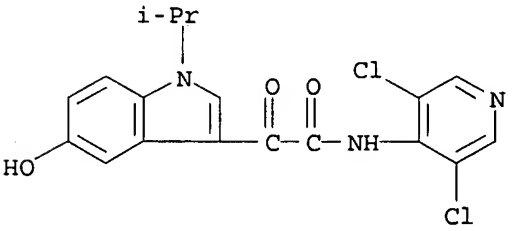
RN 247584-23-2 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



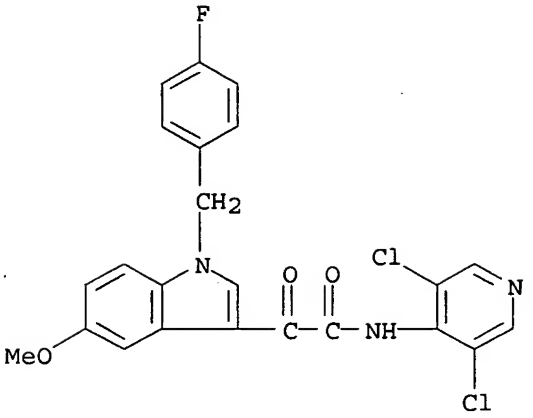
RN 247584-24-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



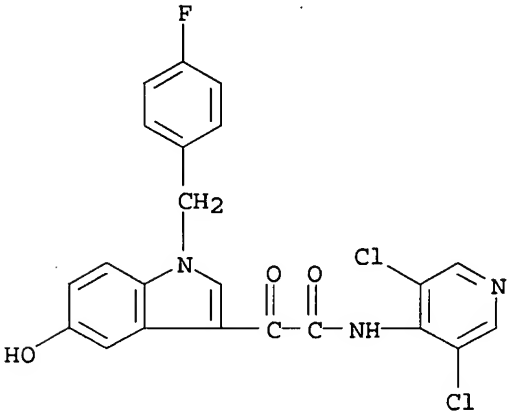
RN 247584-27-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-(1-methylethyl)-α-oxo- (9CI) (CA INDEX NAME)



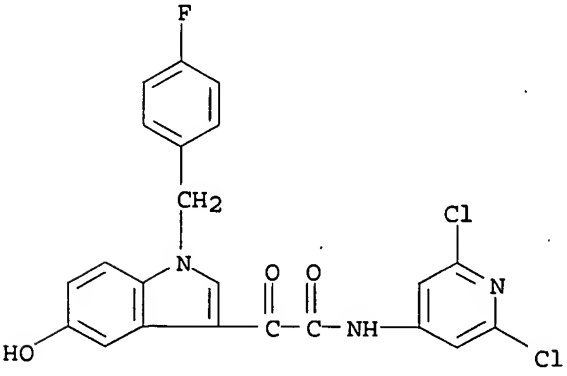
RN 247584-34-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-methoxy-α-oxo- (9CI) (CA INDEX NAME)



RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

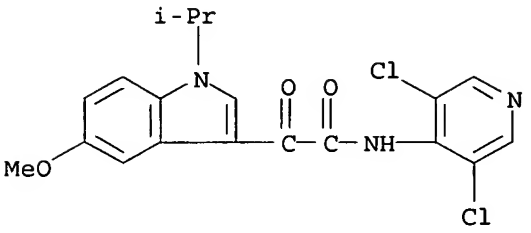


RN 260265-54-1 CAPLUS
CN 1H-Indole-3-acetamide, N-(2,6-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

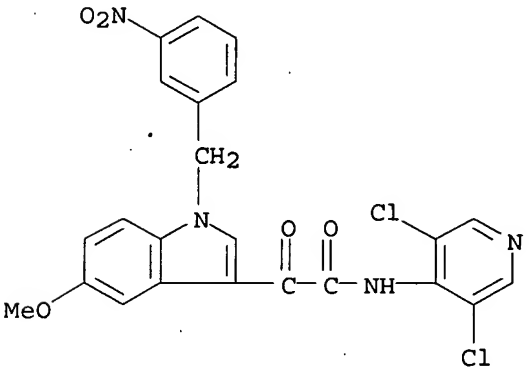


RN 260265-55-2 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-methoxy-1-(1-

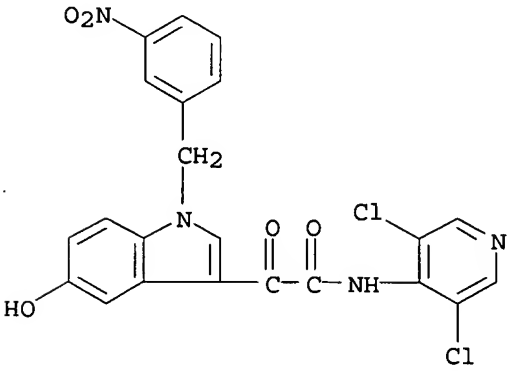
methylethyl)-α-oxo- (9CI) (CA INDEX NAME)



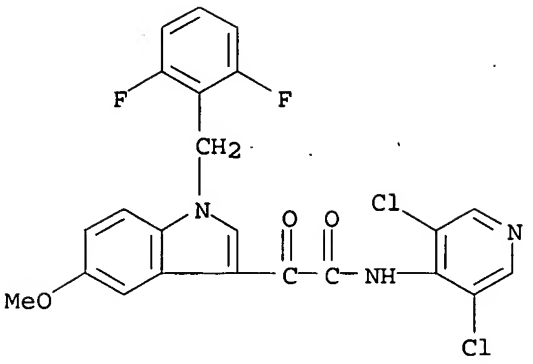
RN 260265-56-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-methoxy-1-[(3-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



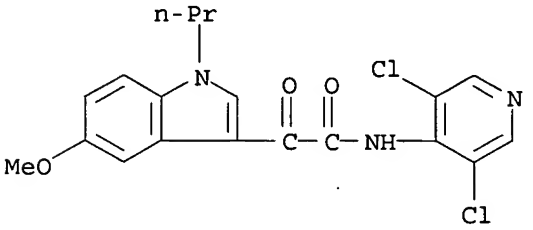
RN 260265-57-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-[(3-nitrophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



RN 260265-58-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-methoxy-α-oxo- (9CI) (CA INDEX NAME)



RN 260265-59-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-methoxy-α-oxo-1-propyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 58 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:708761 CAPLUS
DOCUMENT NUMBER: 131:310549
TITLE: New hydroxyindoles and their use as phosphodiesterase 4 and TNFα inhibitors
INVENTOR(S): Hofgen, Norbert; Egerland, Ute; Poppe, Hildegard; Marx, Degenhard; Szelenyi, Stefan; Kronbach, Thomas; Polymeropoulos, Emmanuel; Heer, Sabine
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955696	A1	19991104	WO 1999-EP2792	19990424
W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19818964	A1	19991104	DE 1998-19818964	19980428
DE 19917504	A1	20001019	DE 1999-19917504	19990417
AU 9938229	A1	19991116	AU 1999-38229	19990424
AU 748403	B2	20020606		

BR 9910029	A	20001226	BR 1999-10029	19990424
TR 200003130	T2	20010122	TR 2000-200003130	19990424
EP 1076657	A1	20010221	EP 1999-920779	19990424
EP 1076657	B1	20040804		
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JP 2002513017	T2	20020508	JP 2000-545856	19990424
NZ 507406	A	20021126	NZ 1999-507406	19990424
RU 2217422	C2	20031127	RU 2000-129678	19990424
AT 272631	E	20040815	AT 1999-920779	19990424
EP 1475377	A1	20041110	EP 2004-18391	19990424
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ES 2222706	T3	20050201	ES 1999-920779	19990424
CA 2270301	AA	19991028	CA 1999-2270301	19990428
US 6251923	B1	20010626	US 1999-300973	19990428
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BG 104842	A	20011031	BG 2000-104842	20001011
NO 2000005454	A	20001207	NO 2000-5454	20001027
HK 1035183	A1	20050415	HK 2001-105669	20010814
US 2002111351	A1	20020815	US 2002-80821	20020221
US 6545025	B2	20030408		
US 2002115651	A1	20020822	US 2002-81395	20020221
US 6545158	B2	20030408		
US 2002119971	A1	20020829	US 2002-81642	20020221
US 2002137745	A1	20020926	US 2002-81807	20020221
US 6602890	B2	20030805		
US 38624	E	20041012	US 2002-176435	20020919
US 2003134876	A1	20030717	US 2003-347659	20030120
US 6613794	B2	20030902		
US 2004220183	A1	20041104	US 2004-856034	20040527

PRIORITY APPLN. INFO.:	DE 1998-19818964	A 19980428
	DE 1999-19917504	A 19990417
	EP 1999-920779	A3 19990424
	WO 1999-EP2792	W 19990424
	US 1999-300973	A3 19990428
	US 2000-653685	A3 20000901
	US 2002-81642	A1 20020221
	US 2002-81807	A3 20020221

OTHER SOURCE(S): MARPAT 131:310549

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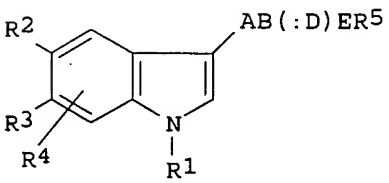


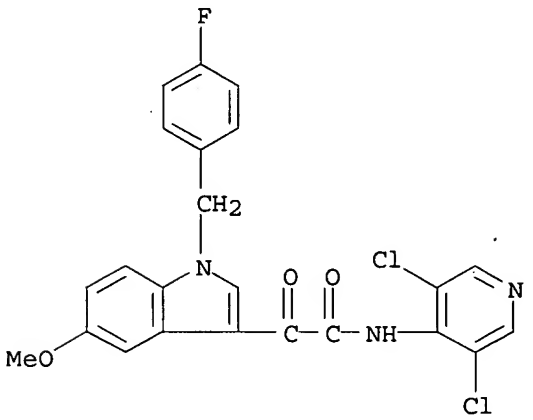
I

AB Hydroxyindoles I [R1, R5 = (un)substituted aliphatic, carbocyclic, heterocyclic, spirocyclic; R2, R3 = H, OH, ≥1 of them being OH; R4 = H, (un)substituted OH, SH, S(O)H, SO2H, NH2, CO2H, C(S)OH, NO2, CN, F, Cl, Br, I; A = alkylene, alkenylene, (CHOZ)m, CO, CS, C:NZ, O, S, NZ; Z = (un)substituted alkyl, alkenyl, carbocyclic, heterocyclic; B = C, S, SO; D = O, S, CH2, NZ; E = bond, (CH2)m, O, S, NZ; m = 0-3] were prepared I have IC50 for PDE IV inhibition of 1X10-9-1X10-5 and a selectivity relative to

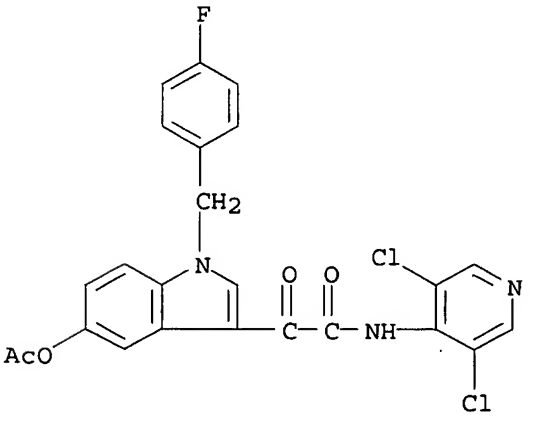
PDE's 2, 3, and 5 of 100-10,000. N-(3,5-dichloro-4-pyridyl)-2-[1-(4-fluorobenzyl)-5-methoxy-3-indolyl]-2-oxoacatamide was obtained by demethylation of the 5-methoxy compound and was reduced to the 2-hydroxyacetamide with NaBH4.

IT **247584-34-5 247584-35-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzylindolylalkanoamides as phosphodiesterase IV and tumor necrosis factor inhibitors)

RN 247584-34-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-methoxy-α-oxo- (9CI) (CA INDEX NAME)

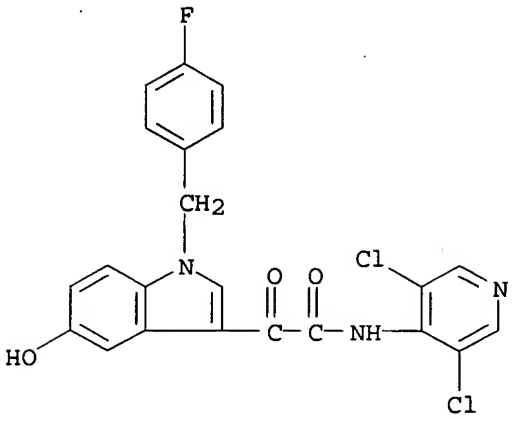


RN 247584-35-6 CAPLUS
CN 1H-Indole-3-acetamide, 5-(acetyloxy)-N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α-oxo- (9CI) (CA INDEX NAME)



IT **257892-33-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzylindolylalkanoamides as phosphodiesterase IV and tumor necrosis factor inhibitors)

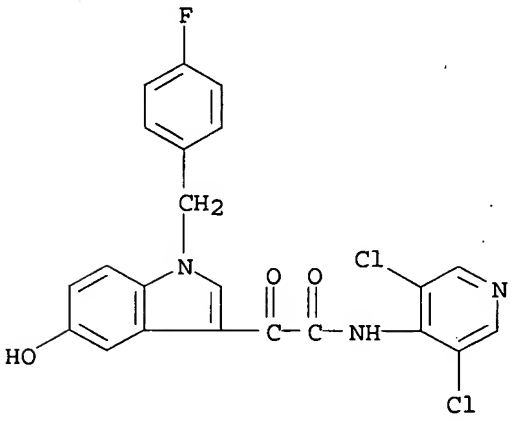
RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



IT **247584-21-0P 247584-22-1P 247584-23-2P**
247584-24-3P 247584-25-4P 247584-26-5P
247584-27-6P 247584-28-7P 247584-32-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzylindolylalkanoamides as phosphodiesterase IV and tumor necrosis factor inhibitors)

RN 247584-21-0 CAPLUS

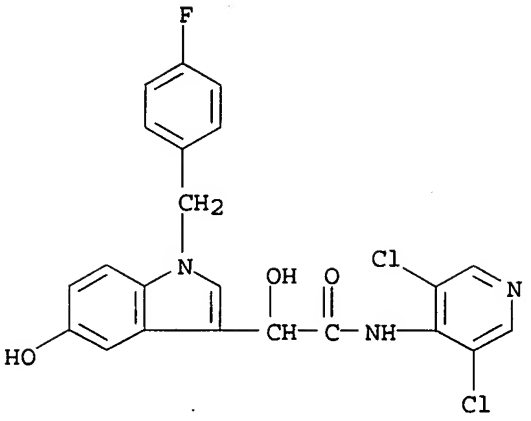
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 247584-22-1 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-α,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 247584-23-2 CAPLUS
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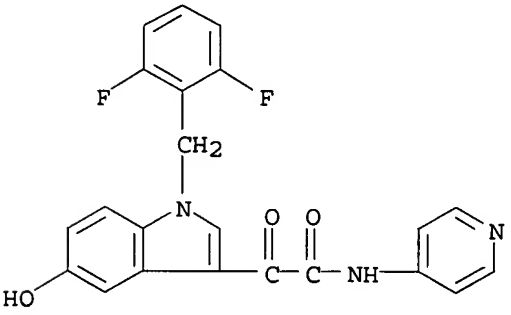
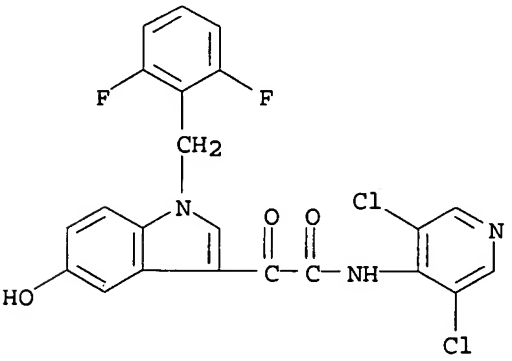
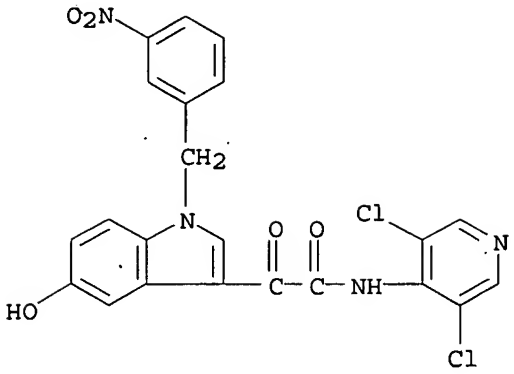


RN 247584-24-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

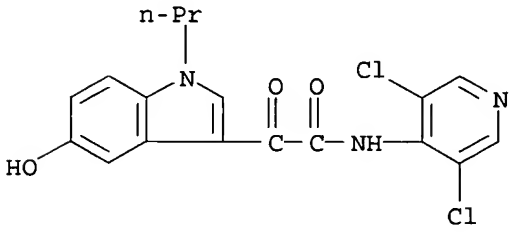


RN 247584-25-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-[(3-nitrophenyl)methyl]-α-oxo-, monosodium salt (9CI) (CA INDEX NAME)

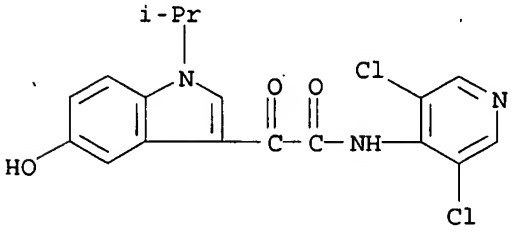


● Na

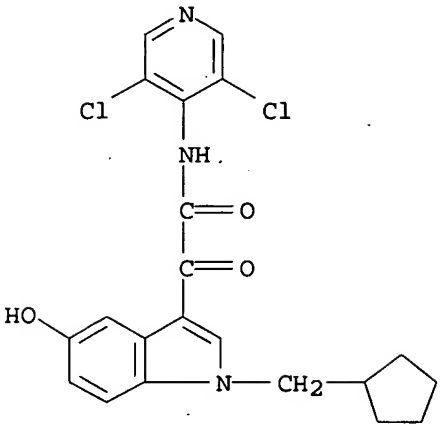
RN 247584-26-5 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-α-oxo-1-propyl- (9CI) (CA INDEX NAME)



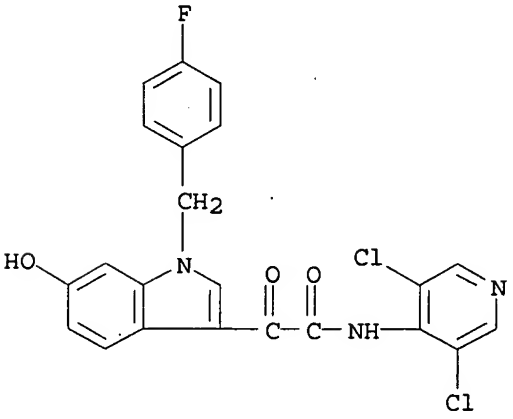
RN 247584-27-6 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-(1-methylethyl)-α-oxo- (9CI) (CA INDEX NAME)



RN 247584-28-7 CAPLUS
CN 1H-Indole-3-acetamide, 1-(cyclopentylmethyl)-N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 247584-32-3 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-6-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 59 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659229 CAPLUS
DOCUMENT NUMBER: 131:271807
TITLE: Preparation of indolylglyoxylamides as antitumor agents
INVENTOR(S): Nickel, Bernd; Szelenyi, Istvan; Schmidt, Jurgen; Emig, Peter; Reichert, Dietmar; Gunther, Eckhard; Brune, Kay
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951224	A1	19991014	WO 1999-EP1918	19990322

W:	AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19814838		A1	19991014	DE 1998-19814838	19980402
DE 19814838		C2	20010118		
CA 2326833		AA	19991014	CA 1999-2326833	19990322
AU 9929349		A1	19991025	AU 1999-29349	19990322
AU 768510		B2	20031218		
BR 9909902		A	20001226	BR 1999-9902	19990322
EP 1071420		A1	20010131	EP 1999-910372	19990322
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002853		T2	20010221	TR 2000-200002853	19990322
EE 200000581		A	20020215	EE 2000-581	19990322
EE 4354		B1	20041015		
JP 2002510622		T2	20020409	JP 2000-541995	19990322
NZ 507084		A	20031031	NZ 1999-507084	19990322
US 6232327		B1	20010515	US 1999-285058	19990402
US 2003114511		A1	20030619	US 2000-492531	20000127
US 6693119		B2	20040217		
NO 2000004916		A	20001201	NO 2000-4916	20000929
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BG 104849		A	20010531	BG 2000-104849	20001012
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US 2003023093		A1	20030130	US 2001-810604	20010319
HK 1036408		A1	20050218	HK 2001-107405	20011024
US 2003195360		A1	20031016	US 2002-309204	20021204
US 2004171668		A1	20040902	US 2003-686809	20031017
PRIORITY APPLN. INFO.:				DE 1998-19814838	A 19980402
				WO 1999-EP1918	W 19990322
				US 1999-285058	A1 19990402
				DE 1999-19946301	A 19990928
				US 2000-492531	A1 20000127
				US 2001-810604	A1 20010319

OTHER SOURCE(S): MARPAT 131:271807

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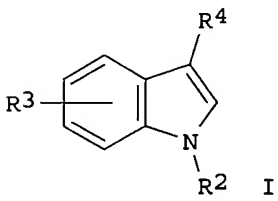


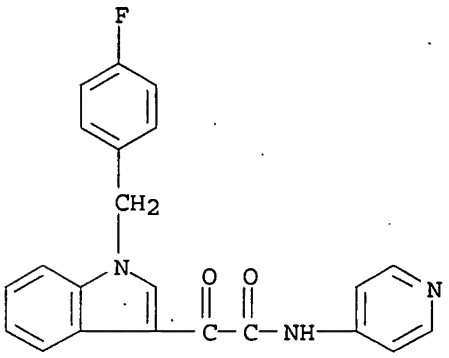
I

AB Title compds. [I; R2 = H or (un)substituted alkyl; R3 = H or 1 or 2 of halo, alkyl, alkoxy, etc.; R4 = C(:X)C(:X)NRR1; R = H, (un)substituted alkyl, CO2CH2Ph, etc.; R1 = (un)substituted Ph, -pyridyl, -pyrimidyl, etc.; RR1 = (CH2CH2)2NR7; R7 = alkyl, Ph, CHPh2, etc.; X = O or S] were prepared Thus, indole was N-alkylated by 4-FC6H4CH2Cl and the product acylated by (COCl)2 to give, after 4-aminopyridine amidation, I (R2 = CH2C6H4F-4, R3 = H, R4 = COCONHR1, R1 = 4-pyridyl). Data for biol. activity of I were given.

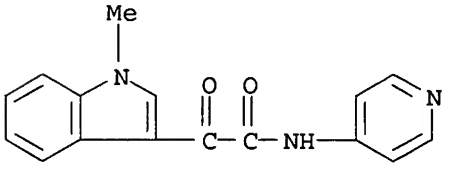
IT **204205-78-7P 204205-79-8P 204205-86-7P 204205-87-8P 204205-90-3P 204205-91-4P 204205-93-6P 204205-96-9P 204205-97-0P 204206-01-9P 204206-03-1P 245661-24-9P**

245661-25-0P 245661-26-1P 245661-28-3P
245661-29-4P 245661-30-7P 245661-38-5P
245661-39-6P 245661-41-0P 245661-42-1P
245661-43-2P 245661-47-6P 245661-48-7P
245661-49-8P 245661-50-1P 245661-51-2P
245661-52-3P 245661-54-5P 245661-55-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolylglyoxylamides as antitumor agents)

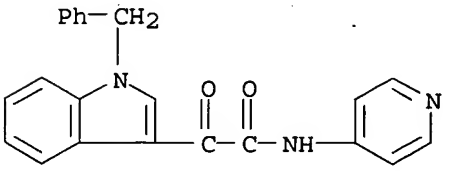
RN 204205-78-7 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



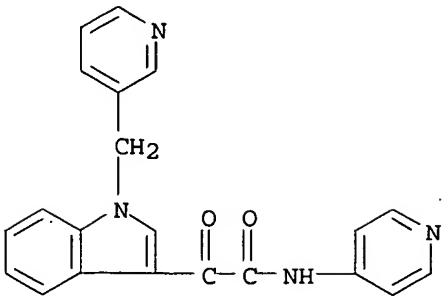
RN 204205-79-8 CAPLUS
CN 1H-Indole-3-acetamide, 1-methyl-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



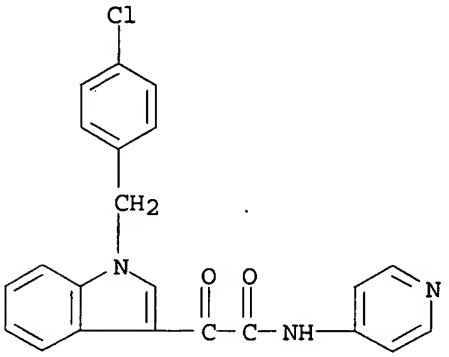
RN 204205-86-7 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-1-(phenylmethyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



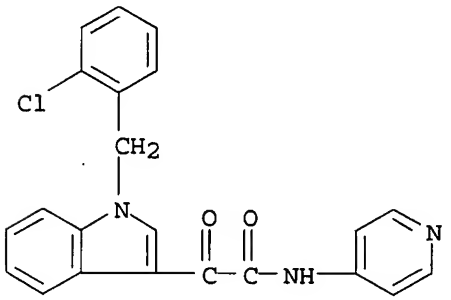
RN 204205-87-8 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-N-4-pyridinyl-1-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



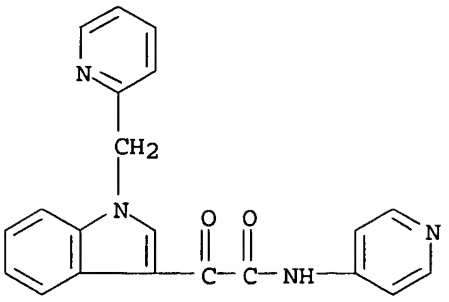
RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



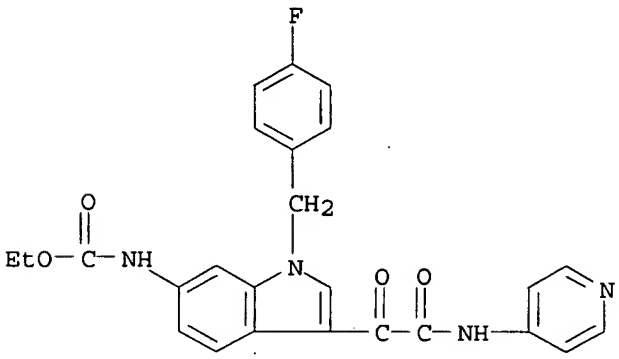
RN 204205-91-4 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



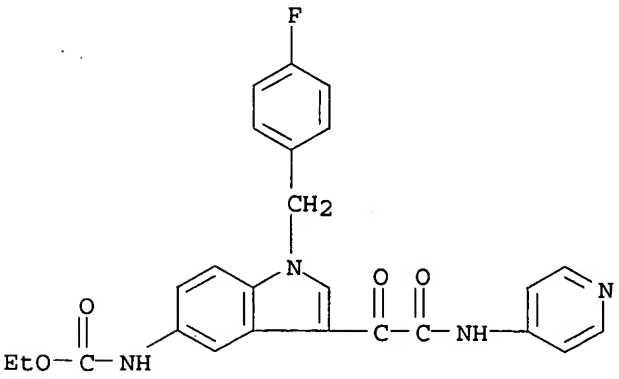
RN 204205-93-6 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-N-4-pyridinyl-1-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



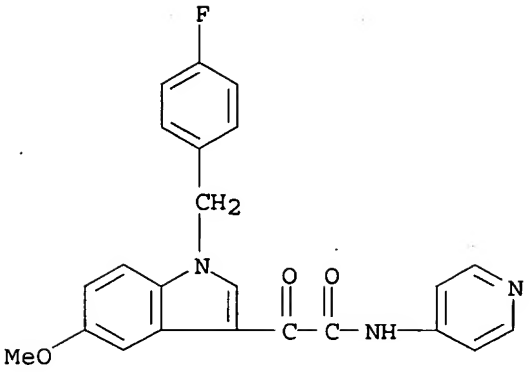
RN 204205-96-9 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-6-yl]-, ethyl ester (9CI) (CA INDEX NAME)



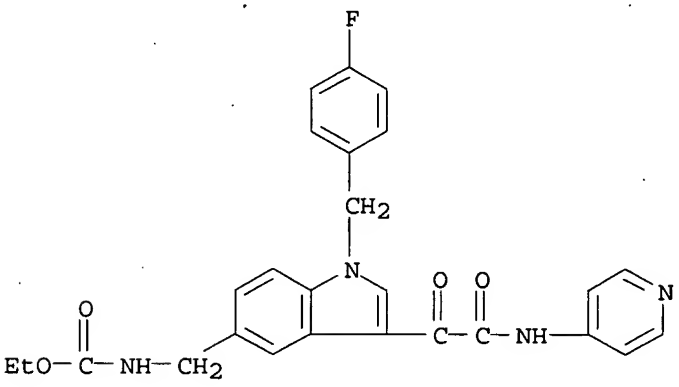
RN 204205-97-0 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]-, ethyl ester (9CI) (CA INDEX NAME)



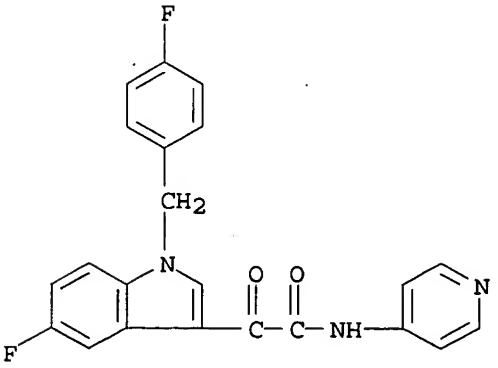
RN 204206-01-9 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-methoxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



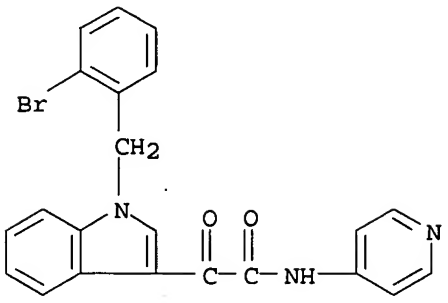
RN 204206-03-1 CAPLUS
CN Carbamic acid, [[1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



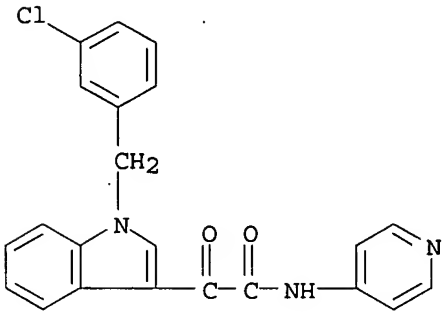
RN 245661-24-9 CAPLUS
CN 1H-Indole-3-acetamide, 5-fluoro-1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



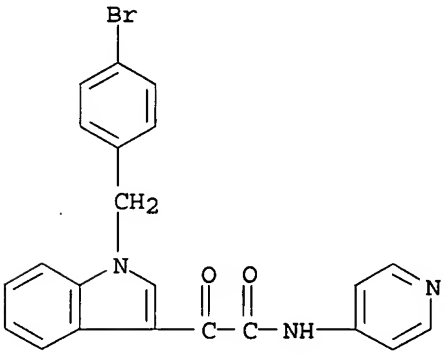
RN 245661-25-0 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-bromophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



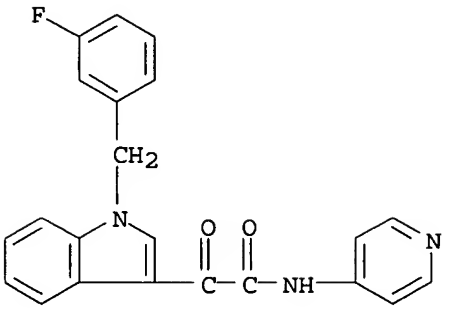
RN 245661-26-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(3-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



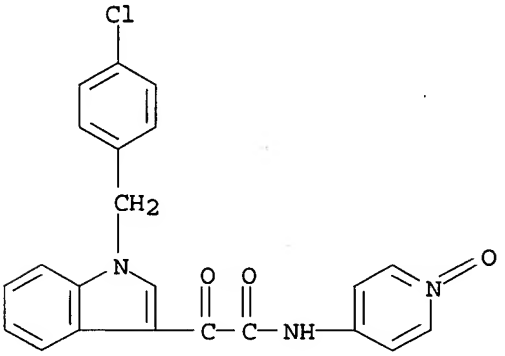
RN 245661-28-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-bromophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



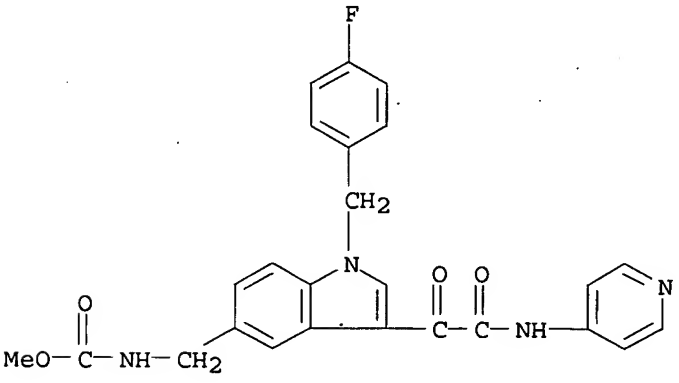
RN 245661-29-4 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(3-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



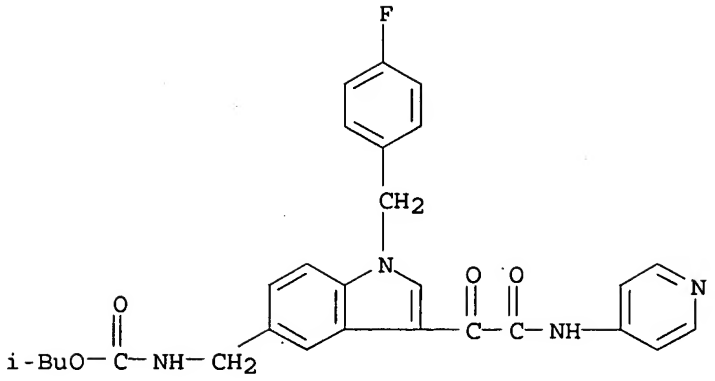
RN 245661-30-7 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-N-(1-oxido-4-pyridinyl)-α-oxo- (9CI) (CA INDEX NAME)



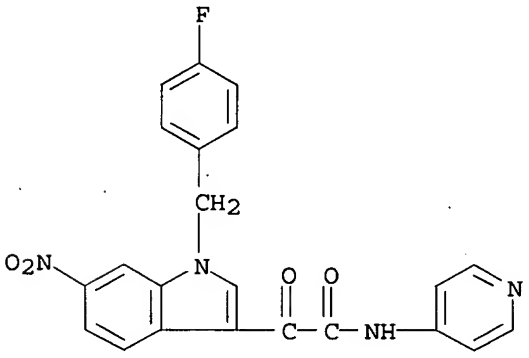
RN 245661-38-5 CAPLUS
CN Carbamic acid, [[1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



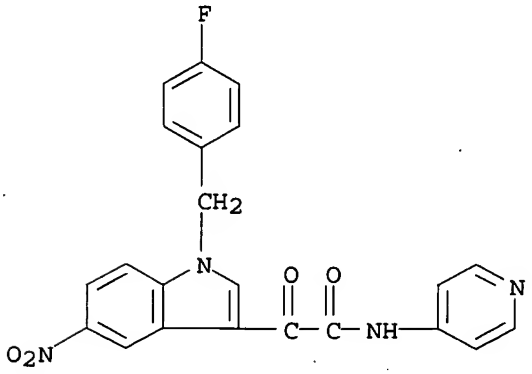
RN 245661-39-6 CAPLUS
CN Carbamic acid, [[1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]methyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



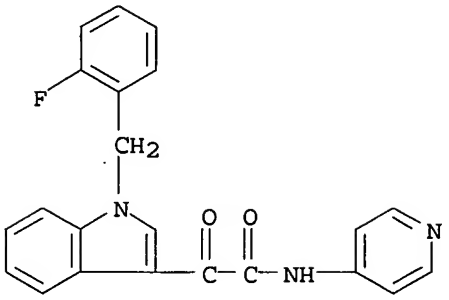
RN 245661-41-0 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-6-nitro-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



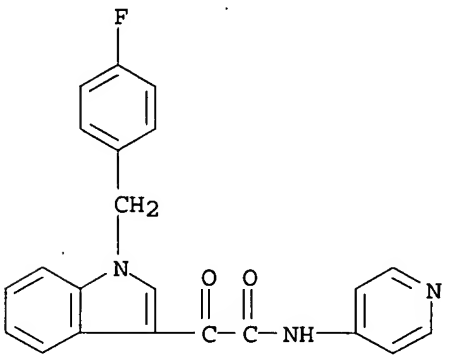
RN 245661-42-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-nitro-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 245661-43-2 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 245661-47-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)

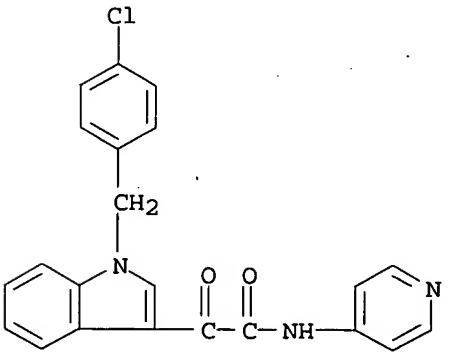


● HCl

RN 245661-48-7 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

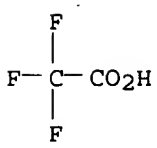
CM 1

CRN 204205-90-3
CMF C22 H16 Cl N3 O2

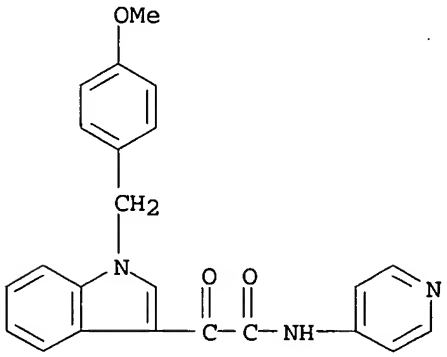


CM 2

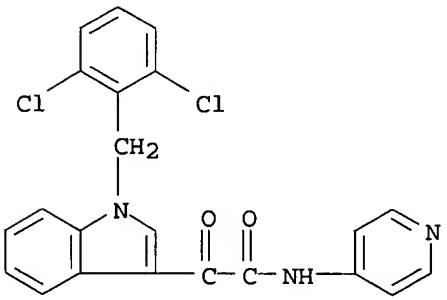
CRN 76-05-1
CMF C2 H F3 O2



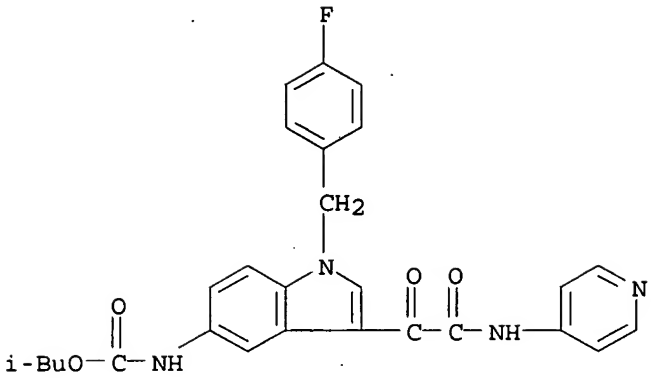
RN 245661-49-8 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-methoxyphenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



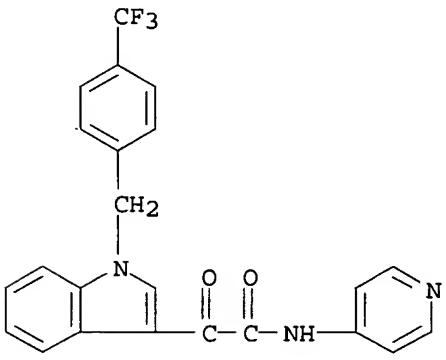
RN 245661-50-1 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2,6-dichlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



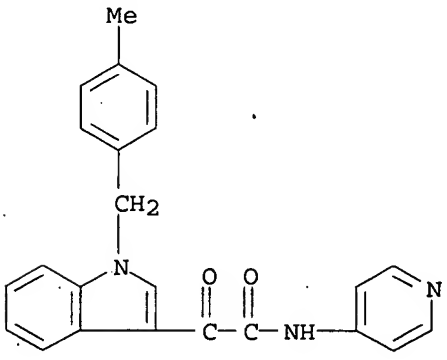
RN 245661-51-2 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



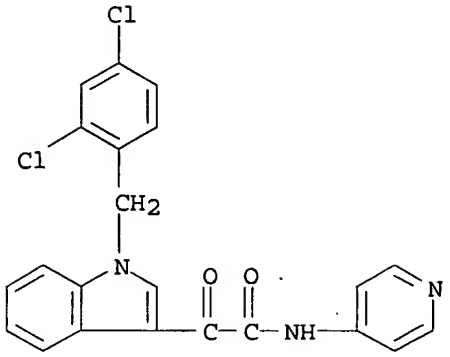
RN 245661-52-3 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-N-4-pyridinyl-1-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 245661-54-5 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-methylphenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 245661-55-6 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2,4-dichlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



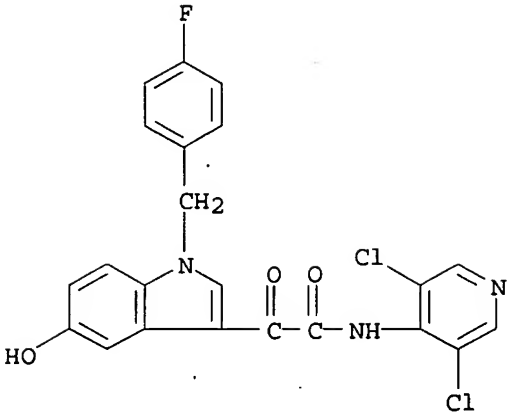
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:647583 CAPLUS
DOCUMENT NUMBER: 132:145941
TITLE: Therapeutic potential of phosphodiesterase 4 inhibitors in allergic diseases
AUTHOR(S): Crocker, I. Caroline; Townley, Robert G.
CORPORATE SOURCE: Creighton University Allergic Disease Center, Omaha, NE, USA
SOURCE: Drugs of Today (1999), 35(7), 519-535
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 137 refs. CAMP is thought to be associated with inflammatory cell activity: high levels tend to decrease proliferation and cytokine secretion, whereas low concns. have the opposite effect (1). Since many phosphodiesterases (PDEs) degrade cAMP, inhibitors of this enzyme decrease inflammatory cell activity. Theophylline, which has nonselective PDE inhibitor activity in addition to its other mechanisms of action, has been used in the treatment of asthma for many years. Unfortunately, because of the important role of PDEs in the cell, nonspecific inhibition of these enzymes causes many undesirable side effects. The discovery of PDE isoenzyme families (PDE1-PDE10), their subtypes (HPDE4 and LPDE4) and their differential distribution among the cell types, as well as their specific functions in controlling cell processes, has led to the development of new, specific PDE4 inhibitors. This review details the rationale for the use of PDE4 inhibitors in the treatment of allergic disease. In addition, the effects of PDE4 inhibitors in vitro, in preclin. animal models and in the clinic are covered. Finally, up-to-date information on the most recently developed inhibitors, such as SB-207499, CDP-840, AWD-12-281 and D-4418, is provided.

IT **257892-33-4**, AWD 12-281
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic potential of phosphodiesterase 4 inhibitors in allergic diseases)

RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

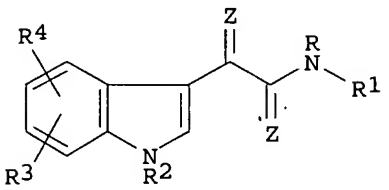
L4 ANSWER 61 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:175908 CAPLUS
DOCUMENT NUMBER: 128:217285
TITLE: Preparation of new, N-substituted indole-3-glyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators
INVENTOR(S): Lebaut, Guillaume; Menciu, Cecilia; Kutscher, Bernhard; Emig, Peter; Szelenyi, Stefan; Brune, Kay
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809946	A1	19980312	WO 1997-EP4474	19970816
W: AU, BR, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SG, SK, TR, UA				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19636150	A1	19980312	DE 1996-19636150	19960906
AU 9740158	A1	19980326	AU 1997-40158	19970816
AU 726521	B2	20001109		
EP 931063	A1	19990728	EP 1997-937586	19970816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1227542	A	19990901	CN 1997-197128	19970816
BR 9712808	A	19991123	BR 1997-12808	19970816
JP 2000505098	T2	20000425	JP 1998-512167	19970816
JP 3296437	B2	20020702		
NZ 334476	A	20000526	NZ 1997-334476	19970816
IL 127798	A1	20030731	IL 1997-127798	19970816
CN 1496980	A	20040519	CN 2002-2002132061	19970816
RU 2237661	C2	20041010	RU 1999-106782	19970816
ZA 9707475	A	19980219	ZA 1997-7475	19970820
CA 2215013	AA	19980306	CA 1997-2215013	19970904
CA 2215013	C	20020305		
US 6008231	A	19991228	US 1997-925326	19970908

TW 550256	B	20030901	TW 1997-86112985		19970930
NO 9901071	A	19990304	NO 1999-1071		19990304
NO 314725	B1	20030512			
US 6344467	B1	20020205	US 1999-409263		19990930
US 2002161025	A1	20021031	US 2002-58836		20020130
NO 2003000481	A	19990304	NO 2003-481		20030130
US 2003207892	A1	20031106	US 2003-402931		20030401
US 6919344	B2	20050719			
PRIORITY APPLN. INFO.:			DE 1996-19636150	A	19960906
			WO 1997-EP4474	W	19970816
			US 1997-925326	A3	19970908
			US 1999-409263	A3	19990930
			US 2002-58836	B1	20020130

OTHER SOURCE(S): MARPAT 128:217285

GI



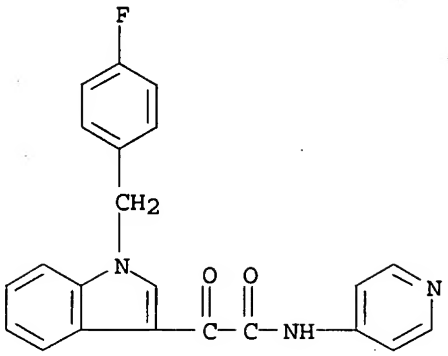
I

AB The title compds. [I; R = H, (un)substituted C1-6 alkyl; R1 = (un)substituted Ph, pyridyl, pyrimidinyl, etc.; RR1 = atoms to close (N-substituted) piperazine ring; R2 = H, (un)substituted C1-6 alkyl, (un)substituted benzoyl; R3, R4 = H, OH, C1-6 alkyl, C3-7 cycloalkyl, halo, NO2, amino, benzyloxy, etc.; Z = O, S] and their acid salts were prepared, e.g., by N-alkylation of indoles with R2-bearing reactants followed by acylation with a dicarbonyl halide and amidation of the remaining acid halide function. For example, a title compound I (R = R3 = R4 = H, R1 = 4-pyridyl, R2 = 4-FC6H4CH2, Z = O) (preparation by benzylation of indole with 4-FC6H4CH2Cl, acylation of the intermediate with (COCl)2 and amidation of the acyl chloride with 4-aminopyridine given) at 10 mg/kg i.p. in guinea pigs gave 55.4% inhibition of allergen-induced late-phase eosinophilia, vs. 47.0 for cyclosporin A.

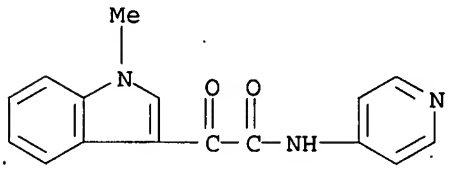
IT **204205-78-7P 204205-79-8P 204205-86-7P**
204205-87-8P 204205-90-3P 204205-91-4P
204205-93-6P 204205-96-9P 204205-97-0P
204205-98-1P 204206-01-9P 204206-02-0P
204206-03-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-substituted indoleglyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators)

RN 204205-78-7 CAPLUS

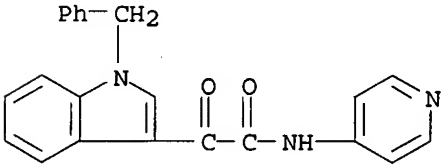
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



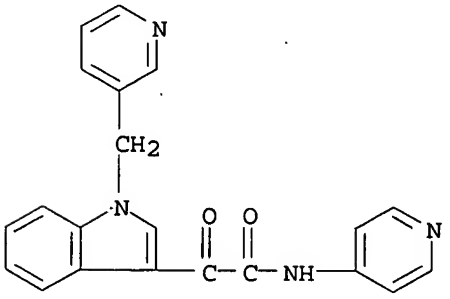
RN 204205-79-8 CAPLUS
CN 1H-Indole-3-acetamide, 1-methyl-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



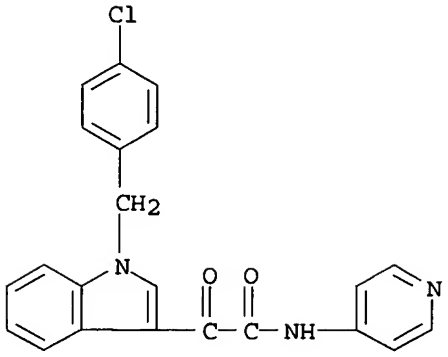
RN 204205-86-7 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-1-(phenylmethyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



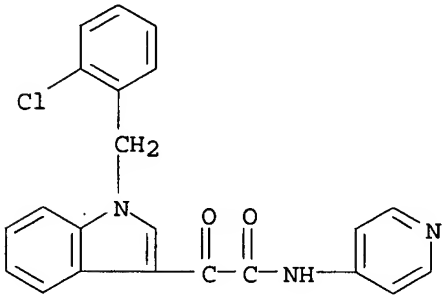
RN 204205-87-8 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-N-4-pyridinyl-1-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



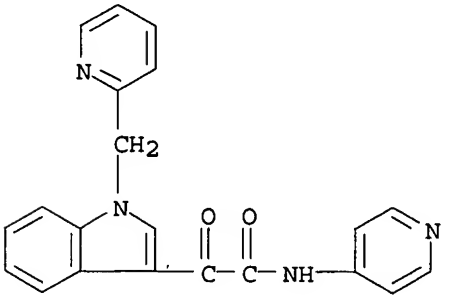
RN 204205-90-3 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



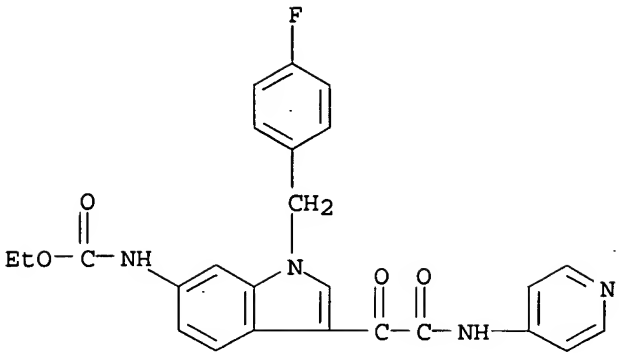
RN 204205-91-4 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(2-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



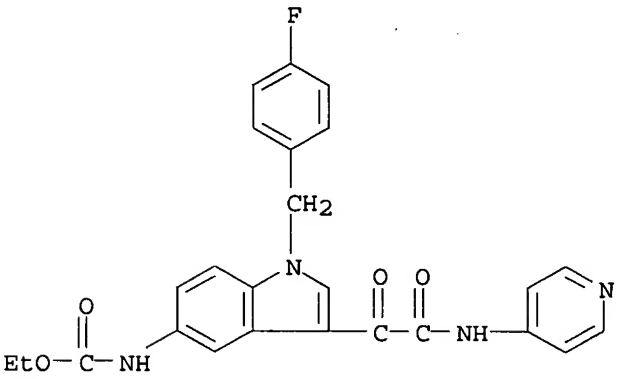
RN 204205-93-6 CAPLUS
CN 1H-Indole-3-acetamide, α-oxo-N-4-pyridinyl-1-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



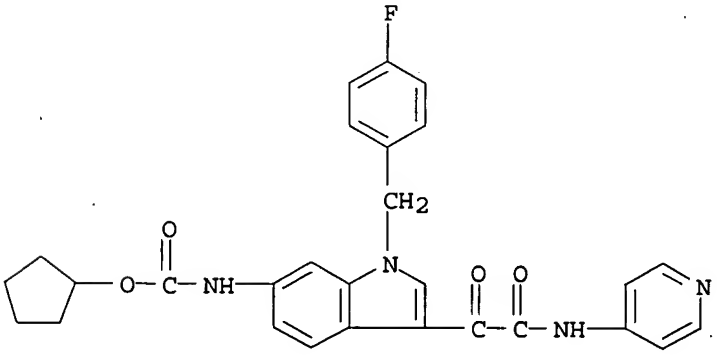
RN 204205-96-9 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-6-yl]-, ethyl ester (9CI) (CA INDEX NAME)



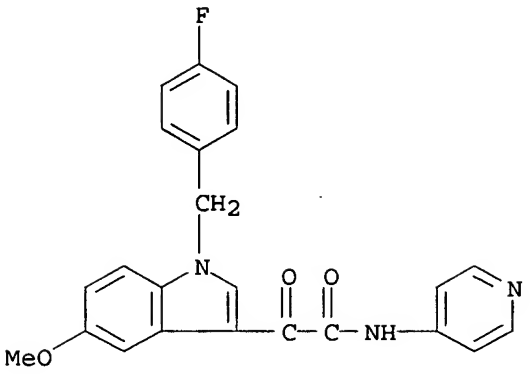
RN 204205-97-0 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]-, ethyl ester (9CI) (CA INDEX NAME)



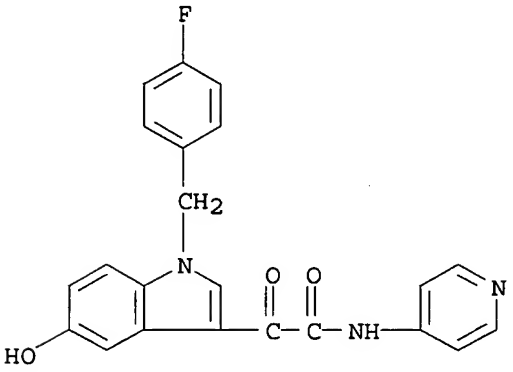
RN 204205-98-1 CAPLUS
CN Carbamic acid, [1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-6-yl]-, cyclopentyl ester (9CI) (CA INDEX NAME)



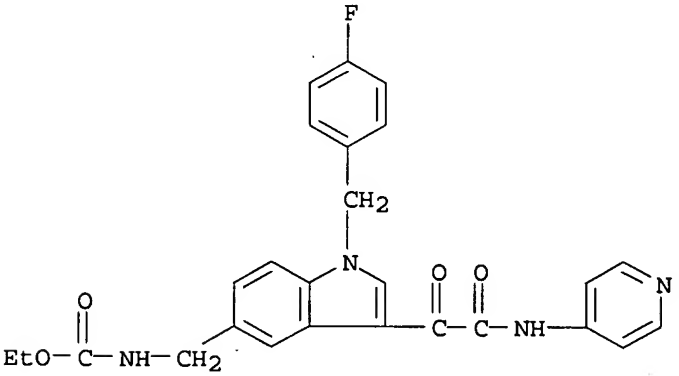
RN 204206-01-9 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-methoxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 204206-02-0 CAPLUS
CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 204206-03-1 CAPLUS
CN Carbamic acid, [[1-[(4-fluorophenyl)methyl]-3-[oxo(4-pyridinylamino)acetyl]-1H-indol-5-yl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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